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QUICK ADJUSTMENTS OF ONGOING GAIT

PERTURBATIONS IN YOUNG AND OLDER ADULTS

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SUMMARY

While we walk around, busy with our daily routines, we rarely consider how complex our gait needs to be in order to handle all the irregularities of our environment. We walk on uneven curbs, avoid puddles of water, pets, running children etc., almost without thinking about it. Even if we lose balance and trip over something, we are often able to recover. This ability deteriorates with aging, when falls become a prominent problem, but one should keep in mind that, if we were unable to adjust our ongoing steps when faced with sudden changes in our environment, falls would occur at any age. Although adjusting step trajectories is crucial for our ability to navigate the environment, it is not known under which circumstances or how this can be accomplished. Therefore, the ability to adjust leg movements during ongoing gait, either perturbed or unperturbed, is the focus of this thesis.

In general, our bodies move by executing motor commands. For example, we decide to 'walk to the sofa' and send this command to our executing elements (i.e., our legs). At the same time the motor command is sent to the legs, its copy is sent to a neural controller called the internal model. The internal model predicts what kind of movement is expected and monitors feedback information from our body and new information from the environment. If there is a mismatch between our movement and what is appropriate and expected, our internal model can determine a movement adjustment is needed. For example, if a cat runs in your path while you are walking towards your sofa, your internal model should act to trigger an adjustment of your step so that you do not step on it. Depending on the situation, sometimes a simple online correction of the ongoing movement is sufficient and sometimes the movement needs to be replaced by a whole new motor plan. In case of walking, our leg swing trajectories are planned in advance based on the visual information from the environment, our goals etc. Therefore, if we encounter a change in the environment our pre-planned step needs to be stopped before an alternative foot landing position can be found.

The objective of this thesis was to provide insights into the ability of humans to adjust leg movements during ongoing gait, both unperturbed and perturbed. The background and rationale for this thesis are described in Chapter 1. Until now, adjustments of ongoing movements were mostly investigated using arm movements or simple leg movements like step initiation, but gait is more challenging, since it is an ongoing movement that poses considerable balance constraints. Furthermore, it is one of the most common daily life activities requiring leg movement adjustments. Therefore, insights into the ability to adjust ongoing gait, both unperturbed and perturbed, might provide useful information in the context of fall prevention and rehabilitation of various patient populations.

In the first part of this thesis we focused on unperturbed gait and developed novel walking tasks in which subjects had to walk on a treadmill by following virtual stepping stones projected onto the treadmill's surface. These stepping stones could change during the approach, forcing the subjects to adjust their precisely aimed steps. This method is described in Chapter 2.

In our first experiment, described in Chapter 3, the stepping stones could change color suddenly, which was an indication they became obstacles to avoid. Therefore, subjects had to adjust their ongoing steps to land outside the obstacle in any way they preferred. Using this task we were able to show that response inhibition (i.e., the ability to stop a movement) plays an important role in obstacle avoidance and we could see that older adults performed worse than young. However, unlike young, older adults also showed learning effects and improved with practice. Furthermore, we paired the walking task with a cognitive task that required inhibition, and found that the performance of both groups deteriorated when the two tasks were performed simultaneously. However, the two groups handled this problem differently and only older adults prioritized their performance on the walking task. Finally, we could see that the difficulties older adults experienced were related to response inhibition, since their performance deteriorated specifically when inhibition was required.

In the second experiment (Chapter 4), instead of changing color, the stepping stones could shift position and subjects had to adjust their steps to follow the stepping stone. Unlike the previous task, this forced subjects to adjust their movements in a specific direction and we found that the direction of stepping stone displacement influenced the accuracy of movement adjustments in young adults. Adjustments were most accurate when step lengthening was required and least accurate for step shortening. Furthermore, the difference in accuracy between step lengthening and shortening became smaller with increasing time pressure. This difference in accuracy suggests a higher risk of unsuccessfully executing a leg movement adjustment when a step is being shortened as opposed to lengthened. Since both step shortening and lengthening are viable options for obstacle avoidance, this difference in risk might affect the way obstacle avoidance strategies are chosen.

In the second part of the thesis we focused on a condition even more challenging than unperturbed gait by investigating the ability to adjust leg movements during tripping. Tripping occurs frequently in our daily lives and leads to falling, unless we are able to make an appropriate recovery step that recovers balance and lands in a safe area. In the final experiment, as described in Chapter 5, we investigated whether it is possible to adjust such steps, which are already adjustments of ongoing gait in order to recover balance, and how this is accomplished. We tripped young adults and presented them with a forbidden landing zone (FZ) at trip onset. Since this FZ was positioned in the area where they would normally land following tripping, they

were forced to adjust the ongoing trip recovery step in order to avoid it. All of our subjects were able to avoid landing in the FZ, but there were individual differences in performance. Some subjects succeeded already in their first trial while others improved over the course of the experiment and succeeded only in the final, fifth trial. Different strategies were used, subjects either shortened their steps or stepped to the side of the FZ. While most subjects used step shortening, shorter subjects tended to step to the size of the FZ, probably because it was positioned too close to the tripping obstacle since their trip recovery steps were shorter. Strikingly, some subjects were even able to switch between strategies. However, irrespective of the strategy used and success of FZ avoidance, balance recovery following tripping was not compromised. Furthermore, we observed strong anticipation effects and subjects adjusted their trip responses even on trials that did not involve a FZ.

Finally, to describe the mechanisms driving these adjustments in Chapter 6 we analyzed muscle activity changes occurring during step shortening, the dominant FZ avoidance strategy. Step shortening was driven by muscle activity changes occurring in two functionally different stages. The first stage of muscle activity change started around 100 ms following trip onset, which is too early to be considered voluntary, and did not contribute to the observed step shortening. Therefore, we suggest this initial stage might have served as a 'pause' until an appropriate movement adjustment was initiated. Second stage of the muscle activity changes occurred at latencies corresponding to voluntary reaction and clearly led to the observed step adjustments (i.e., step shortening and landing on the toes). Interestingly, we found similar muscle activity changes on trials that did not involve a FZ, in line with step adjustments that occurred under the influence of anticipation.

In conclusion, and as discussed in Chapter 7, this thesis shows that it is possible, albeit challenging, to investigate movement adjustments during gait using paradigms common in fundamental arm and eye movement research. These paradigms typically investigate online adjustments and response inhibition separately, but our work demonstrates both are involved in adjustments of gait. In general, our data show that unperturbed and perturbed gait can be modified quickly. Apparently, fast movement adjustments are not only possible for eye, arm, and simple leg movements, but even for extremely challenging whole body movements, such as balance recovery following tripping. Finally, learning effects observed in our experiments show that it is possible to improve leg movement adjustment abilities, which is promising for fall prevention, especially in light of our aging society.

SAMENVATTING

Terwijl we rondlopen, druk bezig met onze dagelijkse routines, zijn we ons zelden bewust van de complexiteit van ons voortbewegen in een onregelmatige omgeving. We lopen op oneffen terrein, ontmoeten huisdieren, stoepranden, plassen water en spelende kinderen. We kunnen deze obstakels vermijden, bijna zonder erover na te denken. Zelfs als we toch ons evenwicht even verliezen, zijn we nog in staat om dat evenwicht snel weer te herstellen. Dit vraagt om het vermogen om tijdig onze stappen aan te passen, wanneer we worden geconfronteerd met plotselinge veranderingen in onze omgeving. Dit vermogen verslechtert echter met het ouder worden, waardoor de kans op vallen toeneemt en een prominent probleem wordt. Het vermogen om stappen aan te passen is, ongeacht leeftijd, cruciaal voor ons voortbewegen. Dit proefschrift is daarom gewijd aan de aanpassingen van beenbewegingen tijdens wandelen, met of zonder balansverstoringen.

We bewegen ons lichaam door motorische commando's uit te voeren. Als we bijvoorbeeld besluiten om naar een stoel te lopen, dan wordt dat bevel doorgegeven aan de spieren in onze benen. Tegelijkertijd wordt een kopie van dat bevel naar een deel van de hersenen gestuurd waar we een "intern model" opbouwen. Dat model kan voorspellen wat de beweging zal zijn en welke sensorische gevolgen er te verwachten zijn. Als er een verschil is tussen die verwachting en de eigenlijke terugkoppeling dan kan het brein besluiten dat er een aanpassing moet plaatsvinden. Stel bijvoorbeeld dat een kat je voor de voeten loopt terwijl je naar de stoel wilt lopen, dan is dat interne model en de sensorische terugkoppeling nodig om je stappen aan te passen zodat je de kat kunt ontwijken. Afhankelijk van de situatie kan een kleine aanpassing van je stap voldoende zijn, maar soms moet het hele motorische plan worden aangepast. Tijdens de zwaaifase van het wandelen is het traject van ons been vooraf gepland op basis van visuele informatie en van het doel dat we willen bereiken. Als er een plotse verandering plaatsvindt dan moeten we in staat zijn om de voorziene stap te stoppen vooraleer een nieuwe plek kan worden gekozen om de voet te plaatsen.

Het doel van dit proefschrift was om inzicht te krijgen in het vermogen van de mens om beenbewegingen aan te passen tijdens wandelen met en zonder balansverstoringen. De aanleiding en het doel van dit proefschrift staan beschreven in Hoofdstuk 1. Tot nu toe werden aanpassingen van geplande bewegingen meestal onderzocht met arm- of oogbewegingen, of in de benen tijdens het maken van een enkele stap. Wandelen is echter meer dan het uitvoeren van een eerste stap. Er ligt een uitdaging om aanpassingen te onderzoeken tijdens het wandelen zelf, vanwege de gevergde balanshandhaving. Maar juist omdat wandelen zo essentieel is in het dagelijkse leven is het belangrijk om inzicht te verwerven over de mogelijkheid om

stappen tijdens het onverstoord wandelen en tijdens balansverstoringen aan te passen. Naast fundamentele kennis kan deze informatie ook gebruikt worden in het kader van valpreventie bij ouderen en voor de revalidatie en het herstel van loopfunctie in patiëntenpopulaties.

Het eerste deel van dit proefschrift is gericht op het wandelen op een loopband en op nieuwe wandeltaken waarbij proefpersonen moesten stappen op virtuele stenen die werden geprojecteerd op een loopband. Deze geprojecteerde stenen konden net voor plaatsing van de voet van kleur of positie veranderen, zodat de proefpersonen de preciese plaatsing van hun voet moesten aanpassen. Deze methode staat beschreven in Hoofdstuk 2.

In het eerste experiment, beschreven in Hoofdstuk 3, kon de steen waarop jongvolwassenen en oudere proefpersonen moesten stappen plots van kleur veranderen. Hierdoor werd de steen plotseling een obstakel wat men juist moest ontwijken. Met behulp van deze taak werd de inhibitie van responsen, oftewel de mogelijkheid om een beweging te stoppen, onderzocht. Dergelijke inhibitie speelt een belangrijke rol in het ontwijken van obstakels. Het bleek dat de ouderen slechter presteerden dan de jongvolwassenen. De ouderen werden bovendien beter gedurende het experiment door oefening, terwijl de jongeren op hetzelfde peil bleven presteren. De wandeltaak werd daarnaast gekoppeld aan een cognitieve taak, die ook inhibitie vereiste. Er werd gevonden dat die koppeling de prestaties van beide leeftijdsgroepen verslechterde. De ouderen gaven meer prioriteit aan het juist uitvoeren van de wandeltaak dan de jongeren, die gelijke prioriteit aan beide taken konden geven. Uit deze studie bleek dat ouderen meer moeite hebben met inhibitie van responsen, wat voornamelijk tot uiting kwam bij het onderdrukken van niet bij elkaar horende responsen.

In Hoofdstuk 4 staat het tweede experiment beschreven, waarbij de stapstenen net voor plaatsing van de voet in positie verschoven. In tegenstelling tot de vorige taak, werden jongvolwassen proefpersonen nu gedwongen om hun bewegingen in een bepaalde richting aan te passen om op het verschoven doel te stappen. De richting van de verplaatsing van de stapsteen was van invloed op de nauwkeurigheid van de beweging. Aanpassingen waren het meest nauwkeurig wanneer stapverlenging nodig was en het minst nauwkeurig voor stapverkorting. Ook werd het verschil in nauwkeurigheid tussen stapverlenging en -verkorting kleiner met toenemende tijdsdruk. Dit verschil in nauwkeurigheid suggereert dat de kans op het succesvol uitvoeren van een beenbeweging kleiner is wanneereen stap wordt verkort dan wanneer een stap wordt verlengd. Dit kan van belang zijn bij het maken van beslissingen wanneer zowel verkorting als verlenging van de stap mogelijk is, zoals bij het vermijden van obstakels.

Het tweede deel van het proefschrift is gericht op een situatie die nog uitdagender was voor de balans dan het wandelen op de loopband en hier is onderzocht of beenbewegingen kunnen worden aangepast tijdens het struikelen. Struikelen komt vaak voor in ons dagelijks leven en kan tot een val leiden, tenzij we in staat zijn om tijdig een aangepaste herstelstap te maken. Voor die herstelstap rijst de vraag of die nog kan worden aangepast op het laatste moment.

In de studie van Hoofdstuk 5 lieten we jongvolwassenen struikelen en toonden hen tegelijkertijd een “verboden landingszone” (VZ) die ze tijdens hun herstelstap moesten ontwijken. Aangezien die VZ overeen kwam met het gebied waar zij normaal zouden landen na struikelen, moesten ze hun herstelstap aanpassen. Alle proefpersonen konden een landing in de VZ vermijden, al waren er individuele verschillen in prestaties. Sommige proefpersonen slaagden er vanaf de eerste poging in om de VZ te ontwijken, terwijl anderen het in de loop van het experiment lukte, soms pas in de vijfde en laatste proef. De proefpersonen gebruikten verschillende strategieën (stap voor, achter of naast de VZ). De meeste proefpersonen verkozen de stap te verkorten; waarbij relatief kleine proefpersonen vaker verkozen om naast de VZ te stappen. Dit komt waarschijnlijk omdat deze personen normaal tijdens het struikelen al een kleine herstelstap zetten en de VZ zo dicht achter het obstakel geprojecteerd werd, dat plaatsing voor de VZ (stapverkorting) lastig mogelijk was. Opvallend was dat sommige proefpersonen zelfs in staat waren om gedurende het experiment van strategie te veranderen. Ongeacht de gebruikte strategie en het succes van het vermijden van de VZ, kwam het herstel van de balans nooit in het geding. De proefpersonen gingen wel steeds meer anticiperen op een VZ en pasten hun herstelstap aan, zelfs in afwezigheid van een VZ.

Om de mechanismen achter deze aanpassingen tijdens struikelen met een VZ te beschrijven, werd voor Hoofdstuk 6 ook een analyse gedaan van de spieractiviteit tijdens de meestvoorkomende strategie, stapverkorting. Stapverkorting werd gedreven door veranderingen in spieractiviteit die zich manifesteerde in twee functioneel verschillende stadia ten opzichte van normaal struikelen. De eerste fase van de aangepaste spieractiviteit vond plaats rond 100 ms na contact met het obstakel; dit is te vroeg om als een vrijwillige activatie te kunnen worden beschouwd. Deze aanpassing in activiteit helpt niet voor het verkorten van de stap en lijkt te dienen als een 'pauze', totdat een passende bewegingscorrectie wordt geïnitieerd. Die passende correctie volgt in de tweede fase van de spieractiviteit, met latencies die overeenkomen met vrijwillige reacties. Deze aangepaste activatie leidt tot het verkorten van de stap en plaatsing van de voet met landing op de tenen. Het was opvallend dat soortgelijke veranderingen in spieractiviteit ook optraden wanneer er geen VZ was maar de proefpersonen zich kennelijk hadden voorbereid op een mogelijk verschijnen van een VZ.

Samenvattend, en beschreven in de algemene discussie van Hoofdstuk 7, laat dit proefschrift zien dat het mogelijk is om snelle aanpassingen in beenbewegingen te maken tijdens het wandelen. Hiervoor werden paradigma's gebruikt die heel dicht aansluiten bij fundamentele studies naar arm- en oogbewegingen, waarbij het gebruikelijk is om apart te kijken naar "online" aanpassingen en naar inhibitie van responsen. In dit proefschrift wordt aangetoond dat beide aspecten van belang zijn bij aanpassingen van het looppatroon. Snelle aanpassingen van een stap tijdens wandelen blijken mogelijk, ondanks de hoge eisen voor balanshandhaving. De leereffecten zoals waargenomen in de experimenten tonen aan dat het mogelijk is om de aanpassingen van de stap te verbeteren. Dit laatste is van bijzonder belang in de context van valpreventie, in het licht van de vergrijzing van de samenleving.

1 GENERAL INTRODUCTION

Our ancestors survived by hunting or gathering food. To be able to do so they had to be able to move through the environment and use sensory stimuli to find food. Additionally, to ensure their survival they also had to avoid, fight or flight potential dangers. The ability to inhibit unwanted movements and adjust them according to the environmental demands is essential for these activities, otherwise one could not pick a fruit from a tree branch that waves in the wind or stop moving towards a predator and run away. Today we survive by different means, but the importance of adaptive movements remains the same. For example, you have to be able to reach the supermarket on a rainy day, avoiding other pedestrians and puddles of mud and, when finally walking down the isle of a supermarket looking for food, you have to be able to use your sensory stimuli to locate the items you need. Additionally, while doing this, you have to adapt to your environment by avoiding suddenly appearing environmental dangers (e.g., a child running to get candy). In short, our survival remains heavily dependent on our ability to stop and adjust unwanted movements in response to the environment.

Movement adjustments and inhibition have so far been widely investigated with a focus on arm movements. On the other hand, the ability to inhibit and adjust leg movements typically receives attention when impaired, for example by various pathologies [1–4] or aging [5–10] . With the aging society this is gaining even more attention due to the huge prevalence and impact of falls [11, 12]. However, one should keep in mind that without the ability to stop unwanted behavior and adjust our movements to environmental demands, falls would occur at any age. Therefore, it is of interest to investigate the overall ability to adjust leg movements, which typically involve different and more demanding balance constraints than arm movements. In the end, while consequences of unsuccessful reaching for a box of cereal might not be dire, tripping over a running child and losing one's balance might result in fall related injuries.

Objective

In this thesis we investigated leg movement adjustment ability during balance challenging situations of unobstructed and obstructed gait, and we explored the underlying mechanisms. Specifically, we investigated the ability to modify foot landing position during an ongoing step in two situations: 1) during precision gait in order to avoid obstacles or follow shifting stepping targets and 2) during balance recovery following tripping in order to avoid landing the recovery step in a forbidden landing zone. We chose these situations because they represent common circumstances during which leg movement adjustments are needed in daily life to either avoid balance perturbations or successfully recover from them. Furthermore, both gait adjustments occur under time pressure and pose considerable balance constraints, especially trip recovery, which might influence the ability or the

willingness of humans to execute movement adjustments. Therefore, our findings provide fundamental insights into the potential of fast control of leg movement adjustments, but also have a practical value since they can inform future research related to fall prevention.

How are movements controlled?

Our movements are consequences of executing motor commands. Although the precise details of how motor commands are planned are not known, the general idea is that a motor command is generated based on our goals, knowledge, past experience, environment, etc., and then sent to our muscles, who execute the desired movement [13]. Once a motor command is sent to execution, two movement control mechanisms are possible. If the control is implemented as an open-loop system the movement is ballistic, i.e., it occurs as a 'one way' process: the motor command is planned and then executed accordingly, without any possibility of adjustment. Alternatively, if the control is implemented as a closed-loop system, relying on feedback information to detect movement errors and adjust the ongoing movement, adjustments to the original motor command are possible.

Closed-loop movement control is accomplished by a system relying on detection of perturbations which might require movement adjustments. If a potential perturbation can be predicted, proactive control can be used to adjust our movements accordingly, and, if not, one has to rely on reactive control to detect ongoing perturbations from sensory input [14]. Changes in the environment can be accounted for by anticipatory control, which relies on sensory input, knowledge and prior experience to predict an upcoming perturbation or reactive control, which detects ongoing perturbations from sensory input [14]. However, executing our own movements can also cause perturbations requiring movement adjustments. This is accounted for by predictive control, which uses forward internal models to predict the effects of upcoming movements on our body [13]. In general, as shown in Figure 1.1, at the same time a motor command is sent to our muscles for execution, its copy is sent to an internal movement model, which uses forward modelling to estimate the resulting body state. This expectation can be combined with other feedback information, both internal and external, to detect potential movement errors and determine if a movement adjustment is needed [13].

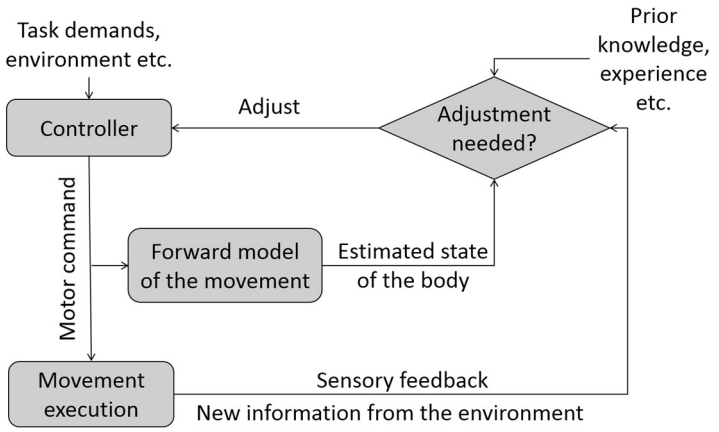

Figure 1.1. General model of closed-loop neural control for movement adjustments, based on [13]. The initial motor command is sent from the neural controller to movement execution. At the same time a copy of the motor command is sent to the forward model of the movement to estimate movement outcomes. Information of the estimated movement outcome (i.e., expected state of the body), sensory feedback, prior knowledge, new information etc. are combined to determine if a movement adjustment is needed and, if needed, the controller can act to implement it.

What is known about arm movement adjustments?

Most previous research on our ability to adjust ongoing movements focused on arm movements and two concepts: online movement corrections and response inhibition. As this thesis will show, both concepts are important for the ability to adjust ongoing gait. Hence, we give an overview of the current knowledge on arm movement adjustment mechanisms, as a basis for our work. Additionally, an extensive overview of the neural control of arm movement adjustments is given in the Appendix (Chapter 9).

Online corrections

Online movement correction research focuses on the questions how movements are adjusted in response to unplanned changes occurring in the environment after the movement is initiated. Humans can adjust their arm movements rapidly in response to changes in the environment [15] or perceived limb position [16]. One of the common experimental paradigms used in these studies is the double step paradigm [15], in which subjects have to point to a target that jumps to change position after the pointing movement is initiated, as shown in Figure 1.2.

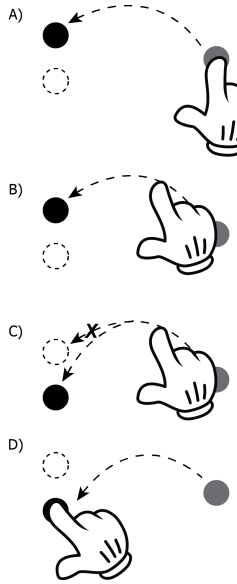

Figure 1.2. Typical double step task. Subjects are asked to point from a starting position (grey circle) to a target (black circle). At trial onset the target is displayed in its initial position (A). Once the movement is initiated (B) the target jumps to a new position and the subject needs to adjust his movement to successfully follow the target shift (C). A successful trial finishes with the subject pointing to the target in its new position (D).

Humans are able to adjust pointing movement direction and amplitude to these target jumps, even when they are not aware the target moved and irrespective of availability of visual feedback on the arm position [15]. Although the precise adjustment onset latencies depend on the algorithms used for their calculation [17], it was consistently shown that such adjustments are very fast [15, 18], and sophisticated in the sense that they match the requirements of the change in the environment. Furthermore, they seem to be irrepressible by conscious voluntary movement adjustments [15, 19], but can be scaled down or inhibited following adaptation to a transformation of visual feedback [20]. Recent research has shown that, irrespective of the required adjustment, pointing movement adjustments start at a fixed latency of about 100 ms and only the intensity of the adjustment is fine tuned to the adjustment magnitude required and time available to complete it [18]. In terms of the underlying mechanisms, forward internal models were suggested to play the major role in early online adjustments [15], while visual and proprioceptive feedback play a role in adjustments occurring at later movement stages [15]. An important aspect to consider is the magnitude of movement adjustment. Small adjustments that can be accounted for using the flexibility of the initial movement are probably controlled by fast processes that do not introduce large increases in movement time. Typically these corrections are characterized by a bell shaped velocity curve with a single peak [15]. On the other hand, corrections in response to large target shifts are suggested to involve decision making and reprogramming of movement, which leads to increased movement times and is characterized by a double peak in the velocity curve [15]. The point at which the switch between the two types of movement corrections occurs and additional reprogramming is needed

is not entirely clear, but probably depends on whether different muscle synergies are needed for adjustment execution, movement velocity, and the timing of the perturbation during movement. Additionally, it is important to note that most research was done using arm movements towards a target, such as reaching to a target or grasping, and it was suggested that reaching might be utilizing a direct and fast subcortical visuomotor mapping [21]. Such fast visuomotor mapping cannot be used for more complex movements (e.g., movements away from the visual stimuli, as are often needed for leg movement adjustments), which probably rely on a slower movement adjustment system [21].

Response inhibition

Response inhibition refers to the ability to inhibit pre-planned or ongoing motor actions and supports flexible behaviors in dynamic environments. It is typically investigated using various computer tasks based on the stop-signal paradigm [22–24] in which subjects have to respond to a 'go' signal unless it is followed by a 'stop' signal instructing them to withhold their response, as shown in Figure 1.3.

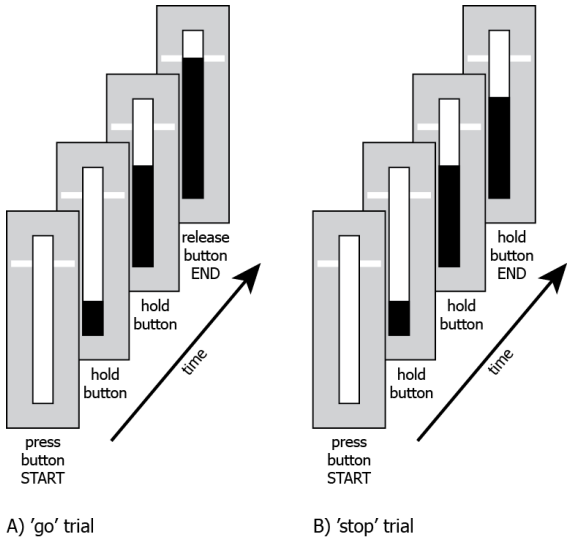

Figure 1.3. Example of an inhibitory task based on the stop-signal paradigm [22, 27, 28, 30]. This task requires the subject to color the empty white bar up to a target level denoted by the horizontal white line. The color filling process is controlled by pressing the mouse button; as long as the mouse button is pressed the coloring continues in the vertical direction, as if the bar is being filled. Once the mouse button is released, the coloring stops. On 'go' trials the task is completely under control of the subject, who prepares and releases the mouse button at an appropriate time. On 'stop' trials inhibition of mouse button release is required if the coloring process stops automatically prior to reaching the target level. In that case the subject is asked to keep the mouse button pressed, i.e., to inhibit the pending mouse button release, until a new trial starts.

This paradigm postulates that the ensuing behavior is the result of a race between the parallel 'go' and 'stop' processes. Whichever finishes first is the one whose behavior prevails (i.e., a movement can be inhibited only if the 'stop' process finishes earlier than the 'go' process). Two models of stopping and going were proposed: the independent race model [23] assumes that the two processes are independent, while the interactive race model [25] assumes their interaction near the end of the race, when the stop process inhibits the go process. Despite their differences, both models result in similar predictions and account for the widely observed behavior: subjects can inhibit their responses when the stop signal is presented soon after the go signal, but they cannot inhibit their responses when the delay between the two signals is large and the go response is close to being executed [24]. More specifically, responses cannot be inhibited when the time needed to complete the stop process is longer than the sum of time needed to complete the go process and the delay between the go and stop signals. Since go processes can consist of a ballistic and a closed-loop stage, and only the closed-loop stage can be modified, the time needed to complete the ballistic stage does not play a role in the time needed to stop a response [24].

Humans use various strategies to increase the chances of successful stopping, both proactively and reactively. Proactive strategy adjustments are made before a trial or series of trials in which the subjects expect stop signals to occur and cause slowing down of the go process reaction times, probably by increasing the response threshold for the go task [26]. Furthermore, proactive strategies facilitate selective inhibition of movement, unlike reactive strategies, which typically involve 'global' response inhibition, i.e. inhibition of all motor output, irrespective of its importance for the task at hand [27, 28]. Reactive strategies also result in slower go process reaction times, occur following trials in which a stop signal was present, and probably reflect a change in goal priorities and memory priming [29]. Reactive adjustments were found both following unsuccessfully inhibited trials, as a result of change towards more cautious behavior, but, surprisingly, also following successfully inhibited trials. Apparently, on successfully inhibited trials the go signals were associated with stopping and thus, when repeated, interfered with the go process. Such effects are long lasting and might lead to development of automatic response inhibition, i.e. to inhibition driven by the bottom-up retrieval of memory associations as opposed to a top-down cognitive initiation of a stop process [24]. Therefore, successful response inhibition seems to be combination of 'automatic' inhibition following memory priming and cognitive control taking into account changing priorities.

Of special interest for this thesis is the stop-change paradigm [24, 31]. The stop-change paradigm is an extension to the standard stop-signal paradigm in which, instead of just stopping, subjects have to replace the go process (go1) with a new

response (the go2 response). This resembles daily life situations in which leg movement adjustments are required, since stopping inappropriate leg movements without execution of an appropriate alternative might lead to balance loss and falling. Research using the stop-change paradigm found that such behavior cannot be completed without a separate stop process (i.e. response inhibition) and that activation of the alternative, go2 response is not sufficient to inhibit the initial, go1 response [31]. Furthermore, the alternative go2 response was found to start only after the stop process finished, indicating either serial processing or parallel processing in which almost all resource capacity is initially allocated to stopping [31]. This was attributed to a strategy choice to reduce the probability of erroneous responses to the initial go1 process and not to structural limitations [24]. However, whether or not stopping indeed needs to be fully completed first is not entirely clear. Namely, using eye and not hand movements, others suggested parallel execution of the stop and go2 processes [32].

Although the stop-signal paradigm is used widely, it is not entirely known whether the same inhibitory mechanism are involved in other inhibitory paradigms. However, several studies comparing behavior on stop-signal, Stroop, Eriksen flanker tasks, and antisaccades suggested a possible common underlying mechanism [24, 33]. Furthermore, while stop-signal tasks are very simple, they appear to recruit a similar brain network as complex stopping tasks [34], which more closely resemble everyday situations. For more details on the neural control of movement adjustments see the Appendix (Chapter 9).

Online movement correction and response inhibition are typically investigated separately, but they probably interact in the process of movement adjustments, even for discrete arm movements such as pointing, which can be stopped without executing an alternative movement. This interaction is even more likely during gait, since gait is a continuous movement and stopping an ongoing step without an alternative foot landing usually threatens balance. During gait, humans plan swing limb trajectories for upcoming steps in a feed forward manner by using visual information about the environment [35]. Therefore, a prerequisite for movement adjustment is inhibition of the pre-planned step, i.e., the pre-planned step needs to be stopped before an adjustment based on feedback information on the surrounding environment [35] and body and limb motion [35] can be executed.

Response inhibition of leg movements

Several groups evaluated response inhibition in the legs using flanker tasks [36] and tasks of perceptual and motor inhibition [37, 38] as cues for step initiation from quiet standing. Incongruent stimuli resulted in an increase in erroneous body weight shifts in preparation for a step (i.e., anticipatory postural adjustments), which had to be

corrected and led to a longer time needed for step execution [38]. This was even more exacerbated when speed of step execution was prioritized over accuracy [36] and in a subgroup of older adults, probably due to inhibitory deficits associated with aging [37]. Taking into account that the speed of step initiation in a choice stepping reaction time test is a strong predictor of falls [39], these findings indicate an important role of response inhibition for daily life mobility. Additionally, response inhibition is an element of executive control, which deteriorates with aging [40–43], is linked to mobility [43–46], and predictive of future falls [47, 48], even up to five years [48]. Specifically, in studies evaluating the effect of executive function on fall risk, measures of cognitive flexibility, set shifting, and task switching were predictive of falls up to two years following measurement [47] and measures of attention and executive function (measured using tests of response inhibition) were predictive of falls up to five years following measurement [48]. In contrast, general cognitive function was not found to predict future falls [47, 48], indicating executive function is not simply a marker of general cognitive aging, but plays a specific role in fall avoidance. Furthermore, response inhibition seems to play an important role for sensory integration, which is a prerequisite of movement. Namely, perceptual inhibition was found to be correlated to postural sway in older adults during conditions of sensory conflict, assumingly because inhibition is needed to modulate the weighting of conflicting sensory information [49].

While this work illustrated the importance of response inhibition for successful initiation of leg movements from standing, the focus of this thesis is on adjustments of ongoing leg movements during perturbed and unperturbed gait, which are more challenging due to time and balance constraints. Such adjustments require a combination of online movement corrections and response inhibition.

Adjustments of leg movements

Leg movement adjustments received attention in various studies focusing on behavior of different groups in a range of tasks, mostly related to research on falls. Less focus was given to the fundamental questions of underlying motor control mechanisms and, unlike arm movement research, there is a lack of widely used experimental paradigms which could help address these issues. Namely, various research groups use various tasks to address the ability to adjust a variety of leg movements. Research most relevant to this thesis is summarized below; for clarity this summary is organized by the type of leg movement adjustment.

Step initiation

Step initiation from quiet stance is probably the least balance challenging of leg movements we execute during our daily lives. Probably due to this fact and the fact that step initiation resembles discrete movements used in arm movement, research

into leg movement adjustment mechanisms translating some of the experimental paradigms used in arm movement research mostly focused on step initiation [7, 50–53]. These studies used the double step paradigm and subjects had to initiate a step towards an illuminated target appearing in front of them. The target could unexpectedly jump in the medio-lateral direction at [50] or after movement onset [7, 51], in which case the subjects had to adjust their foot trajectory in order to land the foot in the new target location. Although these discrete stepping movement adjustments occurred after step onset, in this thesis they are referred to as adjustments of step initiation to indicate the adjusted step started from a standing posture.

Reynolds and Day [50] found young adults were able to successfully execute movement adjustments in response to medial and lateral target shifts of 21 cm occurring at step initiation. Latencies of response to target shifts were very fast and similar to those found in arm movement research [18, 19, 54]; electromyographic (EMG) activity changed after ~97-122 ms and foot acceleration changed after ~114 - 142 ms. However, while adjustments were executed, subjects regularly undershot the targets when positioning their feet. This undershooting was overall more pronounced for medial targets compared to lateral and when no balance support in terms of handrails was given. Additionally, an interaction was found indicating deteriorated ability to execute a medial foot adjustment in absence of balance support, further emphasizing balance as a factor limiting performance. Similar difficulties executing step adjustments in the medial direction were found in stroke patients and healthy controls using the same setup [55]. Although balance limited the extent to which step adjustments were executed, it did not affect the adjustment latencies. The authors suggested a short latency visuomotor pathway for the leg exists, similar to that found for the arm (see Appendix).

Using a similar setup, Tseng and colleagues [7] evaluated the ability of young and older adults to adjust foot trajectory when initiating a step towards a target that could shift laterally by 20 cm. Unlike the previous experiment, target shifts occurred with different latencies (450, 550, or 650 ms) after target presentation, which served as a cue for step initiation. While synchronizing target shifts to initial target presentation and not movement onset was a limitation of the work, authors found similar results as Reynolds and Day [50]: both groups were able to adjust their movements, but targets were mostly undershot. Foot placement errors increased with decreasing time available to respond (i.e., were highest for target shifts after 650 ms, when young adults undershot the target by ~10 cm and older adults by ~12 cm). Latency of responses to target shifts was ~350-250 ms in young adults and decreased for late target shifts, indicating young adults can speed up their responses when needed. This striking discrepancy in latencies compared to the previous study [50] could have been due to a more conservative onset determination criteria and

the speeding up effect could have been a result of the methodology used, i.e., influenced by response intensity. Namely, similar to what was reported as a mechanism of arm movement adjustments [18], intensity of foot trajectory modification in young adults was highest when least time was available (i.e., for late target shifts), which could have resulted in an earlier onset detection time on late target shift trials. Unfortunately, limitations of the experimental paradigm do not allow for a more precise interpretation of response latencies. Yet, this study was able to address age effects on the ability to adjust leg trajectory. Compared to young, older adults took longer to adjust their foot trajectory (~450-500 ms) and were unable to speed up their responses to late target shifts. This was caused by difficulties in step execution and not initiation; older adults were much slower than young during step execution, especially during target shift trials (baseline steps were ~50 ms slower in older adults and target shift trials ~200 ms slower), but only slightly slower (~30 ms) in step initiation. Difficulties of step execution in older adults illustrate that the final outcome of leg movement adjustment relies mostly on the ability to complete this balance challenging task and less on the ability to initiate a movement adjustment at a short latency. Thus, age-related impairments in the ability to adjust foot trajectory during step initiation might be driven by balance constraints associated with execution of the leg movement adjustment. In a follow-up study, the same authors found older adults reduced their foot placement errors following adaptation to predictable target shifts [51].

When step initiation was made more difficult by asking young and older adults to initiate a step over an obstacle and the stepping target jumps in the forward or diagonal positions, subjects were still able to adjust their steps [52, 53]. These adjustments were executed with response latencies of ~175-200 ms in young and 225-300 ms in older adults and, in line with previous work, balance requirements and age might have played a role, as adjustments were less successful in response to diagonal target shifts and in older adults, especially under time pressure.

Gait – precision stepping

Similar to previous studies utilizing double step paradigm during step initiation, Young and colleagues applied this approach during overground walking [8]. Young and older adults with high and low risk of falling were presented with a stepping target that could change position during the approach. The target would jump either medially or laterally requiring leg trajectory adjustments and foot placement accuracy was lower when less time was available for trajectory adjustment and for medial target jumps compared to lateral. Latencies of responses in young adults were longer than previously reported for arms and step initiation (~200 ms) and deteriorated with age (~270 ms in older adults). Once again, balance seems to have played a role in the ability to execute this task, as evident by higher foot placement errors for medial target jumps. Additionally, foot placement errors were higher and

the magnitude of movement adjustment lower in older adults, especially those at a high risk of falling.

Gait - obstacle avoidance

In daily life situations, gait is most commonly adjusted to avoid collision with obstacles. It is therefore not surprising that obstacle avoidance research is abundant. One key difference to previous work on precision stepping during step initiation and gait is in the nature of the adjustment. Namely, while previous work on precision stepping forced the subject to execute a specific movement adjustment, most of the obstacle experiments only present the subject with an obstacle to avoid and allow a free choice of how to do this. These different requirements might result in different adjustment mechanisms. It has been proposed that arm movements to targets are fundamentally different from avoiding obstacles [19, 56].

Obstacle avoidance has been studied using both physical [2, 5, 9, 10, 57–63] and virtual obstacles [64–68] and it was found that without time pressure movement adjustments are easy and spread over multiple steps [67]. In contrast, when time available for obstacle avoidance is limited the task becomes more difficult and one needs to use an online step adjustment, rather than gradual, feedforward scaling of the of the normal step [57]. Therefore, only obstacle avoidance under time pressure is of interest to this thesis.

Unfortunately the majority of obstacle avoidance studies focused on the biomechanics of obstacle crossing, and only to a lesser extent to the underlying neural control. Yet, several interesting observations were reported with respect to the mechanism driving online movement adjustments for obstacle avoidance under time pressure. Overall, both young and older adults were found to be able to adjust leg movements in order to avoid both physical and virtual obstacles [5, 6, 9, 57, 61, 64, 65, 69, 70]. In both groups, rates of success in obstacle crossing increase with more time available to adjust the movement (coined the available response time, ART) [5, 6, 57, 61, 64, 65, 69, 70], but older adults perform worse than young [5, 6, 9, 65]. Several other factors influence time needed for successful obstacle avoidance. Success rates at specific ARTs decrease when subjects are presented with uncertainty of obstacle position [59], are under the influence of alcohol [62], suffer from various pathologies [2, 70–73], or are required to perform a cognitive dual task concurrently [10, 57, 65]. On the other hand, practice [1, 74] and exposure to an auditory startle simultaneously with obstacle presentation [61] were found to improve success rates, i.e. reduce time needed for foot trajectory adjustment.

In line with previously mentioned step initiation research, obstacle avoidance seems to be very fast, occurring at latencies indicating subcortical origin of these responses (see Appendix). More specifically, movement adjustments with latencies of ~120 ms

were found in acceleration profiles [5, 58, 72] and EMG responses [59] of young adults avoiding physical obstacles on a treadmill. Aging had a detrimental effect on these latencies, which were ~150ms in older adults [5, 69, 70, 75]. However, it should be noted this is still faster than simple reaction time of young adults [58] and these short latencies, in combination with the facilitating effect of the startling stimulus [61], suggests subcortical origin of obstacle avoidance responses. On the other hand, when no time pressure is present foot landing position is gradually adjusted several steps ahead of the obstacle, but the precise latency of the first step adjustment is not known [67].

As mentioned before, obstacle avoidance can be achieved in different ways. Most of the abovementioned studies focused on two strategies defined by the behavior of the foot that would contact the obstacle if no adjustment occurs. Specifically, as illustrated in Figure 1.4, step lengthening to step over the obstacle (long step strategy, LSS) and step shortening to step in front of the obstacle before crossing it with the contralateral leg (short step strategy SSS) were reported during overground and treadmill walking [1, 5, 9, 57, 59, 61, 64, 69, 70].

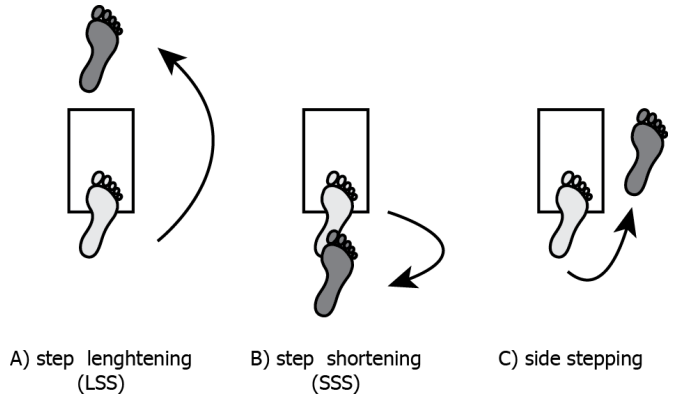

Figure 1.4. Various obstacle avoidance strategies. To avoid an obstacle one can change the preplanned foot landing position (light gray) and implement an alternative foot landing (dark gray) to avoid collision. Steps can be either lengthened (long step strategy, A), shortened (short step strategy, B), or side stepping can be used (C).

Which of these is used for obstacle avoidance is not random and appears to depend on several criteria, namely minimal displacement from the normal foot landing position, stability, and maintenance of forward progression [67, 76]. The priority of these criteria is suggested to change depending on the number of steps available for movement adjustment [67]. When threatened, stability and safety appear to be prioritized more [5, 9, 66, 76] and when very little time is available for obstacle

avoidance subjects tend to switch from LSS to SSS [9, 64], presumably because SSS is easier to implement. However, several discrepancies in the reported data indicate that ART cannot be the sole parameter driving the strategy selection. For example, older adults [9, 69] and stroke patients [70] underutilize, while cerebellar patients over utilize the SSS [1] compared to young controls. It has been suggested that using a stereotyped strategy (e.g., LSS in older adults) might be a way to eliminate the associated choice cost [9]. However, another study reported that decision making associated with choosing an avoidance strategy did not increase the time needed for its implementation [76]. Thus, precise mechanisms driving strategy selection for obstacle avoidance remain to be determined. Strikingly, the presence of an auditory startle during obstacle avoidance was found to cause a significant increase in the use of LSS [61], indicating the involvement of subcortical structures in strategy selection.

The potential influence of balance constraints on obstacle avoidance has not been investigated directly, but it seems balance plays a role in the way obstacle avoidance is achieved. This follows from several studies reporting differences in behavior between healthy young adults and groups with possible balance impairments, such as older adults [5, 9, 63], especially fallers [5]. Strategy selection or conservative obstacle avoidance biomechanics are often attributed to the prioritization of safety [1, 5, 9].

Unlike previously reported experiments, a study by Moraes and colleagues [66] differed in the methodology. Similar to others, they used obstacles located in the predicted foot landing area during overground walking to force a leg trajectory adjustment. However, on a number of trials directional cues (arrows) inside the obstacles forced the subjects to execute a specific avoidance strategy. Subjects were required to avoid the obstacle by a step in the direction of the arrow and latencies of responses ~290 ms were found, indicating cortical involvement. The authors attributed such long response latencies compared to previous work [50, 58] to the obstacle being static and participants possibly relying more on the preprograming of the movement, rather than online correction. Subjects had to process the arrow cue and position their foot accordingly, for which cortical involvement might be necessary. Interestingly, on a number of trials subjects aborted their initial, preferred response in order to follow the cued direction. Additionally, with respect to strategy choice, forced movement adjustments were most successful in the direction that was predominantly chosen during unforced obstacle avoidance; i.e., when, presumably, inhibition would be required the least.

Tripping

When obstacles cannot be avoided and collision of the swing leg with the obstacle results in a trip, adjustments of the ongoing, perturbed step are usually attempted in order to regain balance and avoid falling. Several groups successfully elicited

tripping perturbations in the laboratory setting by using physical obstacles or ropes to obstruct the forward swing of the leg during gait [77–88] and fast movement adjustments for balance recovery were reported.

Two main recovery strategies (Figure 1.5) were identified for balance recovery following obstruction of the swing leg: subjects either elevate the obstructed foot over the obstacle to take a recovery step ('elevating') or lower it in front of the obstacle and use the contralateral leg for the recovery step ('lowering') [85]. These two are reminiscent of LSS and SSS used for obstacle avoidance and, similarly, it remains unknown which factors drive the decision making process. Elevating is typically used for trips elicited in early swing, while lowering occurs as a response to late swing tripping [77, 78, 85]. However, both strategies occur in response to mid swing trips, indicating that time of impact is not the only factor driving this decision [78].

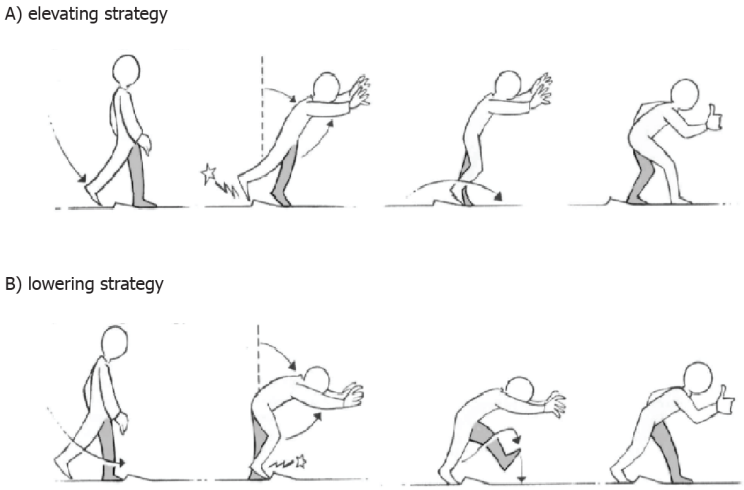

Figure 1.5. Strategies used for trip recovery. An elevating strategy (A) consists of taking a recovery step by lifting the tripped foot over the obstacle, whereas a lowering strategy (B) consists of lowering the tripped foot and taking a recovery step with the other leg. With permission [92].

While the decision making mechanisms remain unknown [89, 90], it seems that the process of trip recovery occurs in two stages [78]. Namely, when subjects perform elevating and lowering in response to a trip occurring in the same swing phase [81] or switch between trip recovery strategies in response to the environment [78] the initial EMG response, starting ~60 ms following trip onset, seems to be the same

irrespective of the recovery strategy used. Only the second stage of the EMG response, occurring after ~100 ms, is strategy specific. Similar is found for the kinematics, which are the same until ~150 ms after trip onset. Such two stage responses might provide sufficient time for choosing a strategy appropriate for successful trip recovery under the given circumstances.

More specifically, balance recovery following tripping begins with short latency EMG activity to stiffen the ankle joint and functional adjustments of EMG activity occur at latencies of ~60-120 ms [77–79, 83–85, 91]. Balance requirements of these movement adjustments were addressed in a study combining step initiation with a trip, in which young adults were tripped during step initiation with and without balance support provided by hand railings [84]. When balance support was available, moving the limb was the only priority and muscle responses were fast (<100 ms) and of lower intensities than when balance was unsupported. When balance was unsupported, responses were of higher magnitude and required an additional correction to prevent destabilization, indicating movement adjustments were influenced by balance and stability and safety were prioritized. Strikingly, although the availability of balance support influenced their behavior, subjects did not utilize it and loaded the handrails with only ~1-2N in total.

Can gait adjustments be further modified?

An additional question to be raised is whether the movement adjustments mentioned above are susceptible to further fine tuning during their execution. More specifically, are these corrections open-loop (non-modifiable) or closed-loop (modifiable) movements [93]? Several studies on obstacle avoidance and tripping suggested the possibility of closed-loop actions since they demonstrated examples of the ability of young adults to adjust corrective leg movements that were already adjustments of normal gait in response to additional perturbations in the environment [78, 84, 94, 95]. The ability to adjust obstacle avoidance reactions after they were initiated was reported in a number of experiments [66, 94, 95]. For example, when young adults were required to avoid a stationary obstacle and, on a number of trials, a second obstacle, either high or low, suddenly appeared during the initial obstacle avoidance step two-stage movement corrections were found [94]. In this case nonspecific heel trajectory adjustments started ~120 ms and were followed by fine tuning related to obstacle height occurring ~280 ms following the second obstacle's appearance. Similarly, when young adults avoided static obstacles that could either increase or decrease in size one step prior to crossing, lead limb elevations were modified using a default response and the trail limb elevation changed accordingly to the resizing of the obstacle, possibly due to the longer time available for trail leg movement adjustments [95]. While these examples highlight the ability to scale gait movement adjustments, gait movement adjustments can also be inhibited. Moraes and colleagues [66] reported young adults could abort an

ongoing obstacle avoidance step, when it conflicted with the instructed obstacle avoidance direction, and switch to a step adjustment that was instructed. Similarly, several subjects were incidentally reported to abort an ongoing trip recovery step and switch to a different trip recovery strategy [78, 89, 90], probably in order to reduce the risk of falling.

Outline of the thesis and research questions

This thesis describes a number of studies aimed at investigating the ability to adjust leg trajectories of ongoing steps in response to visual cues during gait and during balance recovery following tripping. In line with these different situations, this thesis consists of two parts: part one addresses step adjustments during gait in order to avoid suddenly appearing obstacles or follow shifting stepping targets, while part two focuses on step adjustments during trip recovery.

Part 1: step adjustments during precision gait

The main research question we addressed in the first part of the thesis was whether response inhibition plays a role in gait adjustments for obstacle avoidance and how aging affects these gait adjustments for obstacle avoidance. We hypothesized response inhibition would be needed for obstacle avoidance and that aging would have a detrimental effect on obstacle avoidance, especially when response inhibition is stressed. To answer these research questions we tested the performance of young and older adults using a novel walking task based on the stop-signal paradigm. This task, which stressed response inhibition, was paired with an auditory Stroop task, a cognitive task requiring response inhibition to correctly respond to some, but not all, auditory stimuli. Hence, the auditory Stroop task did not interfere with visual processing needed for walking, but could interfere with inhibitory requirements of the walking task, providing valuable information on response inhibition during gait adjustments for obstacle avoidance. Finally, we wanted to investigate whether forcing a specific direction of step adjustment influences its success and hypothesized that gait adjustments would not be equally successful in all directions. This was tested using another novel walking task, based on the double step paradigm.

The system we utilized for the first part comprised an instrumented treadmill and a generic projector (C mill, Forcelink, Culemborg, the Netherlands) to project visual stepping stones to subjects walking on a treadmill. These stepping stones were linked to the subjects' gait pattern and could change color or position to trigger leg trajectory adjustments at various gait cycle times. Subjects were required to either avoid stepping on stepping stones suddenly changing color (Chapters 2 and 3) or follow stepping stones that shifted position (Chapter 4).

Chapter 2 focuses on **development of a novel walking task which stressed the inhibitory requirements of obstacle avoidanc**e. Subjects were required to walk on a treadmill by stepping on virtual stepping stones, which could suddenly change color to indicate they became obstacles to avoid. This task was inspired by the stop-signal paradigm used in arm movement research and stresses response inhibition because steps to be modified were initially aimed at the stepping stone that turned into an obstacle. Task difficulty can be modified by adjusting the position at which the change from target to obstacle occurs. The closer the target is to the subject at time of color change, the more difficult the task, because step to be stopped and adjusted is further along. Chapter 2 shows that this novel test can be used to assess the level of motor inhibition during walking in young adults and establishes a protocol to use in older adults.

Chapter 3 describes an experiment in which **this novel task**, termed precision step inhibition (PSI) task, **was used to test the behavior of young and older adults** under single and dual task condition. Combining the PSI task with a cognitive task targeting inhibition enabled us to show inhibitory requirements related to obstacle avoidance on the PSI task. Since obstacle avoidance and inhibitory abilities both decline with age, potentially leading to increased incidence of falls, we compared the ability of older to that of young adults in order to address several issues. Firstly, we wanted to know if it is possible to use the PSI task in older adults and compare their abilities to those of young adults. Secondly, we wanted to evaluate the inhibitory requirements of the PSI task and the auditory Stroop task which was used for dual tasking. Finally, we wanted to evaluate the interference of these two tasks requiring inhibition and were interested in age related differences in task prioritization.

Chapter 4 takes a slightly different approach to investigating leg movement adjustments during gait. In this chapter the focus is not on avoiding obstacles, but on **following shifting stepping targets** (double step paradigm, see above). Young adults were required to walk on a treadmill by following stepping stones, which served as stepping targets. In case a stepping stone suddenly shifted position subjects had to adjust their leg trajectory in order to land on the target successfully. By manipulating the direction and timing of stepping stone shifts we tested the roles of direction and temporal constraints on leg trajectory adjustments. We evaluated the accuracy of the executed adjustments to see if movement adjustments in different directions represent different levels of difficulty and wondered if this might be one of the reasons for different strategies used for obstacle avoidance.

Part 2: step adjustments during trip recovery

The second part of this thesis focuses on adjustments of leg movement trajectories during balance recovery following tripping. In the second part of the thesis, our main research question was whether it is possible to adjust balance recovery responses

and if so, how this is accomplished. We hypothesized that young adults would be able to adjust their trip recovery steps by shortening or lengthening their recovery steps, without jeopardizing their recovery success. Once again we used a novel experimental paradigm, which forced young adults to adjust their balance recovery responses in order to avoid a forbidden landing zone (FZ) during tripping. Similar to the first part of the thesis, we used a generic projector to show visual context to trigger leg movement trajectory adjustments in order to avoid a virtual obstacle. However, now this occurred during trip recovery, which poses increased balance requirements compared to walking. Young adults were unexpectedly tripped during overground walking and, on a number of random trials, presented with a FZ at trip onset. This FZ was located at each subject's preferred recovery step landing position and, in case the FZ was presented, subjects had to avoid landing into it. Therefore, the FZ served as a virtual obstacle forcing an adjustment of the trip recovery step in order to land the recovery foot elsewhere. Effects of trip response adjustments on balance recovery were quantified in terms of the angular momentum of the body around its center of mass, which indicates whether normal and adjusted trips generated similar amounts of balance perturbation (angular momentum at trip onset), how much of this perturbation was counteracted during the tripping response (angular momentum at landing), and whether the residual perturbation presented balance recovery problems following recovery step landing (angular momentum 0.3. s after landing). Additionally, we quantified the rotation our subjects experienced throughout the recovery step as the area under the angular momentum curve. While we quantified angular momentum as a continuous measure of balance, we did not quantify stability, usually evaluated using biomechanical measures addressing the ability to recover from perturbations or reflecting the maximal perturbation one can handle [96]. Hence, throughout this thesis we use the term 'stability' in a broad sense, as the ability to avoid falling. Finally, we analyzed the underlying muscle activity to investigate mechanisms driving trip recovery adjustments.

Chapter 5 aimed to establish **whether tripping responses can be adjusted and how this affects balance recovery**. Behavior of young adults is described in terms of step strategies and their characteristics, while consequences for balance recovery are described in terms of angular momentum at trip onset, recovery step landing, and following recovery step landing. Finally, behavior on 'catch' trip trials, during which no FZ was shown, is described in the same way to illustrate the role of anticipation.

To understand behavior it is essential to study the output of the motor system. **Chapter 6** provides insight into the process driving leg movement adjustments following tripping by **analyzing muscle activity changes underlying step shortening**, the most common strategy used by young adults for avoidance of the FZ described in Chapter 5. This chapter describes changes in muscle activity driving step

shortening and evaluates whether these muscle activity changes consist of functionally separate components with respect to shortening the recovery step. As in Chapter 5, performance on 'catch' trip trials is analyzed to address the role of anticipation on the process of leg movement adjustment which results in step shortening.

The thesis ends with a **general discussion**, **Chapter 7**, which highlights the main findings of this work, addresses its limitations and suggests future research directions.

PART 1: STEP ADJUSTMENTS DURING PRECISION GAIT

2 RESPONSE INHIBITION DURING AVOIDANCE OF VIRTUAL OBSTACLES WHILE WALKING

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Abstract

While walking, one often has to suppress and adjust a planned step in order to avoid a fall. Given that steps are preprogrammed this requires some form of motor inhibition. Motor inhibition is commonly tested in hand function and only recently attempts have been made to evaluate inhibition in the lower limbs, during step initiation. As adequate motor inhibition might play a role in avoiding falls a test to assess response inhibition during walking would be valuable. We developed a task in which subjects walked on a treadmill by stepping on projected patches of light, which could suddenly change color forcing the subjects to avoid it by shortening or lengthening their steps. The difficulty level was manipulated in 4 conditions by changing the distance available to respond. We hypothesized that larger demands on motor inhibition during walking would produce more failures and tested the performance of young adults (n = 12) in order to establish the protocol for use in older adults. The failure rate on the walking test was analyzed. Reducing the available response distance by 150 mm from the easiest condition resulted in a significant increase in failure rates from 15.6% to 65.1%. Therefore, results indicate this novel test can be used to assess the level of motor inhibition during walking. Additionally, in comparison to previous literature on obstacle avoidance, our experiment shows that changing a precise aiming movement is considerably more challenging than changing the same movement executed automatically.

Keywords

Response inhibition, obstacle avoidance, precision stepping, gait, accidental falls

Introduction

During walking humans plan swing limb trajectories in advance [35]. In case of a perturbation, one needs to inhibit the preplanned step and find an alternative foot landing position to avoid instability and falling.

Response inhibition in the lower limbs has been assessed during quiet standing [49] and step initiation [7, 38, 39], showing that impaired ability to modify voluntary step initiation contributes to the risk of falling [7, 39] and that motor inhibition is required for a timely onset of a voluntary stepping reaction [38]. However, these experiments focused mainly on movement preparation [38, 39] while most falls occur during walking [12], which is a continuous activity more demanding than step initiation.

Therefore, in the present pilot study we developed a task to measure the ability to modify an ongoing movement during walking using an obstacle avoidance (OA) task. Similar to the work of Chen et al. [6, 64, 65], we used virtual obstacles projected on a treadmill. However, in our case the subjects aimed to step on virtual stepping stones. These stones could suddenly change to obstacles, thus stressing the need to inhibit an ongoing step. Hence our unperturbed steps were precision steps, while the perturbed steps required these precise aiming steps to be suppressed and adjusted.

We hypothesized that larger demands on motor inhibition during walking would produce more failures and tested the performance of young adults in order to establish the protocol for further use in older adults.

Methods

The experiment was approved by the local ethical committee according to the declaration of Helsinki and twelve young adults (22.58 ± 2.5 years, 5 women) without musculoskeletal problems or vision impairments participated after signing informed consent forms.

Subjects walked on the C-Mill treadmill (ForceLink, Culemburg, the Netherlands) at a speed of 3 km/h by stepping on patches of light that served as stepping stones. If a stone suddenly changed color it was to be considered an obstacle and subjects were instructed to avoid it by either shortening or lengthening their step. Color changing stones were randomly distributed and their position was defined by the available response distance (ARD), the distance between subject's center of pressure and a virtual line in front of the subjects (Figure 2.1).

Task difficulty was increased by decreasing the ARD. Depending on individual step length, the phase of the step cycle could differ for any given ARD. The largest between subject difference in average step length was 8 cm meaning that, given the

speed of 3 km/h and a step cycle of 1 s, there could be a change of about 10% of the step cycle for any given ARD condition (Table 2.1 shows data on step lengths).

Following gradual introduction to the task, the starting level difficulty was determined by performing short versions of the task (three obstacles per level) starting at a very easy ARD (600 mm) and increasing difficulty until the first failure. This was repeated and the mean ARD at which the two failures occurred served as individual starting level.

The protocol consisted of a baseline condition (walking without obstacles) followed by 4 conditions with increasing difficulty. The individually determined starting level was used for the easiest condition and for the subsequent conditions the ARD was decreased each time by 50 mm. Each condition consisted of 20 obstacles that could appear on both sides of the treadmill, at a frequency of 7 per minute.

Failure rates were calculated from video recordings of the experiment by dividing the number of failures by the total number of obstacles presented. Following a Shapiro–Wilk normality check the data were analyzed with a GLM repeated measures ANOVA and Tukey HSD post-hoc tests using Statistica 11 (StatSoft, Tulsa, OK, USA). Level of statistical significance was set at $\alpha = 0.05$.

Table 2.1. Average step lengths and individually determined „easy“ level ARD values per subject. Step lengths were calculated from recorded reflective marker data as half of the distance between two consecutive left heel strikes and averaged for each subject.

subject	*step length [m]*	*"easy" ARD [mm]*
1	0.54	450
2	0.53	600
3	0.54	450
4	0.52	500
5	0.53	500
6	0.58	550
7	0.50	450
8	0.53	500
9	0.54	550
10	0.54	600
11	0.53	550
12	0.53	550
AVERAGE	0.53	520.8
SD	0.02	51.9
MIN	0.50	450
MAX	**0.58**	**600**

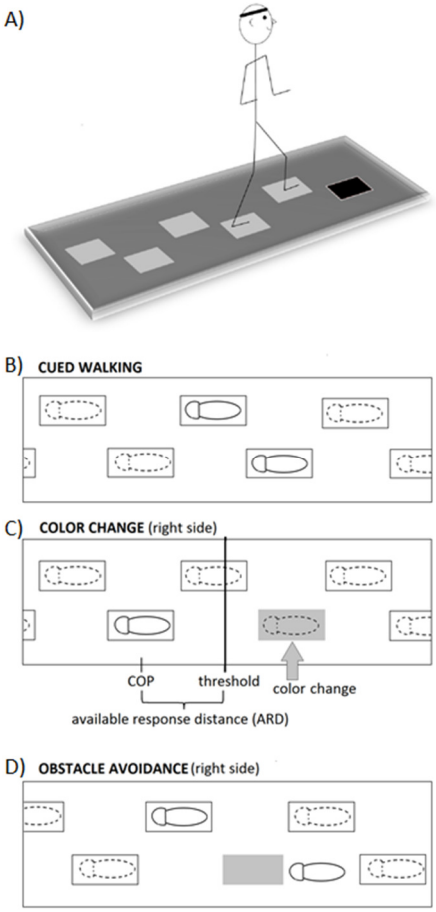

Figure 2.1. Experimental setup and conditions. Subjects walked on the C-Mill (ForceLink, Culemburg, the Netherlands), a system comprising a projector and an instrumented treadmill with stepping stones projected relative to subjects' gait (a). This system can detect foot contacts, predict subsequent steps, and, based on this, project gray patches of light (serving as stepping stones) onto the treadmill. Distance between the stepping stones (i.e. step length) was individually adjusted to be comfortable and was held constant during the experiment. The subjects were instructed to walk and step on the stones (b), unless a stone changed color from gray to purple (c). In the latter case the purple stepping stone was to be considered an obstacle and subjects were instructed to avoid it by either shortening or lengthening their step (d). Stepping to the side of the obstacle or on it was considered a failure. The change in color could appear in front of any foot, at a frequency of 7 per minute. The timing of color changes was randomly distributed and the position of the stone to color was defined by the available response distance (ARD). ARD is the distance between subject's center of pressure and a virtual line in front of the subjects (c). The first stepping stone ahead of this line changed color. Hence the stepping stone that was about to change color could be situated just behind this virtual line or at an additional distance, corresponding to the distance between the virtual line and the position of the stepping stones. Maximum possible distance was therefore 'ARD + step length' and dependent on individual's step length, while the minimal distance was defined by ARD.

Results

Results are shown in Figure 2.2. Subjects had a gradient in performance matching the increasing difficulty, although individuals differed in their ability to perform at a given ARD. Repeated measures ANOVA revealed main effects of difficulty ($F = 80.57$, $p < 0.001$). Increasing difficulty significantly increased failure rates for all conditions (Tukey HSD, all $p < 0.001$).

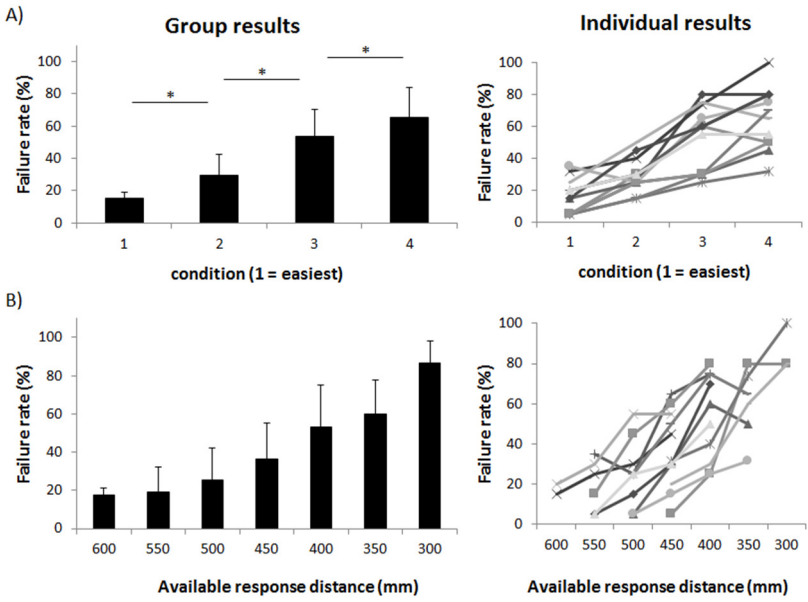

Figure 2.2. Average group results (n=12) and individual failure rates per condition (2a) and available response distance (2b). Condition 1 is the easiest and the difficulty is increasing in subsequent conditions. Decreasing the available response distance increased the difficulty of the task. Error bars denote standard deviations. * indicates statistical significance of the task ($p < 0.05$).

Discussion

We presented a novel test for assessing response inhibition during walking, in which subjects needed to unexpectedly modify precision aiming steps. Healthy young adults showed consistent increases in failure rates at their individually tailored difficulty levels, proving that the test is sensitive to measure response inhibition as function of task difficulty.

Our test is novel in that previous tests have focused on gait initiation rather than on ongoing gait [7, 38, 39]. Nevertheless, there are similarities. During step initiation about 5 times more failures were found for a 200 ms available response time (ART) decrement [7] while we found about 4 times more errors (15.6% and 65.1%) for a 150 mm ARD decrement (equivalent to 180 ms ART at a speed of 3 km/h).

Similarly, it is of interest to compare the present work on precision stepping with studies on avoidance of physical [5, 57] and virtual [64, 65] obstacles. These studies used ART, defined as the time between obstacle release and the predicted moment of the contact with the obstacle if there would be no avoidance reaction. They found

success rates approaching 100% at ARTs around 350 – 450 ms for both overground [64, 65] and treadmill walking [5, 57]. In contrast, our subjects did not reach a 100% success rate with ARDs of 600 mm (an equivalent of 720 ms ART). This may be explained by differences in the methodology and task complexity. Our subjects aimed to step on the stone before it turned into an obstacle and had to suppress and adjust this precise aiming movement, which was not the case in the previous OA studies. Additionally, our obstacles could randomly appear on both sides, while previously they would either be projected across the whole walkway [64, 65] or only on one side of the treadmill [5, 57]. If the same obstacles could appear at either side on a treadmill a significant response latency increase was reported [59]. These differences underline the fact that the present task is more challenging than previous OA tasks. Apparently, it takes substantial time to change an ongoing motor plan for a precise aiming step and this ability deteriorates when the time to respond decreases.

In the present experiments, increasing difficulty levels were used sequentially rather than randomly. This sequence was chosen because starting with trials in which they failed very frequently was very demotivating for the subjects during pilot experiments. In principle, this sequential order could have resulted in fatigue effects. To verify this point we repeated the “easy” condition at the end of the series in one subject. If fatigue played a role one would expect the failure rate to be higher in the repeated “easy” condition but the failure rate did not differ (15% in both cases). The sequence could in principle also have induced learning effects. However, this would have led to improvements in performance over time and clearly this was not the case.

It is concluded that the present task is appropriate for testing response inhibition during precision stepping and can safely be used to assess changes in response inhibition in elderly.

3 RESPONSE INHIBITION AND AVOIDANCE OF VIRTUAL OBSTACLES DURING GAIT IN HEALTHY YOUNG AND OLDER ADULTS

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Abstract

Adjustments of preplanned steps are essential for fall avoidance and require response inhibition. Still, inhibition is rarely tested under conditions resembling daily living. We evaluated the ability of young and older adults to modify ongoing walking movements using a novel precision step inhibition (PSI) task combined with an auditory Stroop task. Healthy young (YA, n=12) and older (OA, n=12) adults performed the PSI task at 4 individualized difficulty levels, as a single and dual task (DT). Subjects walked on a treadmill by stepping on virtual stepping stones, unless these changed color during approach, forcing the subjects to avoid them. OA made more failures (40%) on the PSI task than YA (16%), but DT did not affect their performance. In combination with increased rates of omitted Stroop task responses, this indicates a "posture first" strategy. Yet, adding obstacles to the PSI task significantly deteriorated Stroop performance in both groups (the average Stroop composite score decreased by 13% in YA and 27% in OA). Largest deficit of OA was observed in rates of incorrect responses to incongruent Stroop stimuli (OA 35% and YA 12%), which require response inhibition. We concluded that the performance of OA suffered specifically when response inhibition was required.

Keywords

Obstacle avoidance, older adults, dual task, response inhibition, Stroop task, accidental falls

Introduction

During gait, we plan swing limb trajectories for steps ahead using visual information about the environment in a feed forward manner [35]. If perturbed, one needs to adjust a planned step using feedback information both on whole body and limb motion [35] and on the surrounding environment [35, 97]. This requires inhibition, because the preplanned step needs to be stopped before finding an alternative foot landing position. Therefore, inhibition is an important skill, lack of which might lead to increased instability and risk of falling, especially given the age related deterioration of inhibitory abilities [98, 99].

In the past, response inhibition ability was typically tested in the arms [22, 28]. More recently however, several groups have attempted to assess response inhibition in the lower limbs in healthy older adults (OA), thereby attempting to bridge the gap with the field of arm motor control [7, 38, 49, 100]. These experiments have confirmed a link between inhibition and motor reactions, more specifically postural sway and step initiation.

With respect to gait it is interesting to relate these findings on response inhibition to falls. It is known that falls are associated with an impaired ability to execute a fast voluntary step [39]. This impairment might be due to inhibitory deficits as it has been shown that inhibition of inappropriate postural adjustments is required for a timely onset of a voluntary stepping reaction [38, 100]. Furthermore, the ability to modify an initiated step in response to desired foot landing position shifts declines with aging [7]. However, these experiments remain somewhat remote to circumstances of falling. They focused mainly on movement preparation [38, 39, 100] and were limited to step initiation, while most falls occur during walking [11, 12]. Therefore, we aimed to measure the ability of OA to modify ongoing movements during walking. To this aim, we used an obstacle avoidance task [5, 68], as a common fall related situation, and included an element of inhibition in order to work in parallel with the arm movement experiments on response inhibition. Our specific walking task required stepping towards a precise target and then inhibiting that step following a sudden “stop” signal [101]. This is a form of obstacle avoidance that stresses the need for inhibition and adjustment of preplanned steps as the obstacles initially represent targets for subjects to step on. Hence, this walking task requires inhibition of ongoing precise steps and we refer to it as precision step inhibition (PSI) task throughout this paper. Our previous work established a protocol that proved to be feasible, although demanding, in young adults (YA) [101]. However, it remains to be seen whether this task is appropriate for use in OA, the population of interest with respect to falls.

To further test for response inhibition we added a cognitive dual task (DT) that also requires inhibition. Including a DT in our experiment is not only interesting from the

inhibition point of view, but also adds ecological validity with respect to falls. During daily living one almost always performs multiple tasks while walking, and with advancing age even simple cognitive tasks can have a detrimental effect on postural stability and obstacle avoidance [57, 102–104]. Indeed, cognitive decline has been associated with an increased risk of falls [48, 105] and some studies suggested that changes in DT performance are significantly associated with an increased risk for falling amongst OA [106–108]. The auditory Stroop task [10, 57, 109] is especially suited in this context, since subjects respond to congruent and incongruent stimuli, but only incongruent stimuli require inhibition. Therefore, evaluating the performance in response to the two types of stimuli separately provides insight into inhibitory demands and capacities, while at the same time controlling for dual tasking per se, similar to the methods used by others [49]. Finally, a DT experiment allows for inferences about task prioritization. If response inhibition is “global” [28, 110], i.e. inhibitory resources are shared for the two tasks, we should be able to see task interference. Furthermore, if the PSI task is prioritized over the Stroop task, the subjects’ performance on the Stroop task would deteriorate, while the PSI task performance would remain stable. On the other hand, if there is no clear prioritization, the performance on both tasks would suffer under DT conditions. It has been suggested that OA use a "posture-first strategy", prioritizing stability in demanding conditions [111–113]. A similar strategy was observed in stroke patients under conditions of obstacle avoidance [75]. However, for obstacle avoidance in healthy OA, some previous experiments reported that adding a DT affected the success of obstacle avoidance [10, 57, 65], whereas others observed no DT effect, although they reported subtle changes in gait speed and stride length, probably due to ample time available for preparation for obstacle avoidance [109]. The question remains whether healthy OA would prioritize posture more when the obstacle avoidance task is made more difficult, for example by adding an aspect of response inhibition. This would go in line with the suggestion that prioritization is a dynamic process, dependent on the difficulty of the tasks involved [102, 103]. Hence it is important to use demanding motor and cognitive tasks if one wants to gain insight into task prioritization.

To summarize, the aim of this study was threefold. Firstly, to assess the feasibility of using the newly developed PSI task in OA and to compare their performance to the previously reported performance of YA (Potocanac et al., 2014). We expect OA to have more difficulty performing the PSI task, which should be reflected in higher failure rates and more time needed for successful obstacle avoidance. Secondly, to evaluate the inhibitory requirements of the Stroop tasks by evaluating the performance in response to congruent and incongruent Stroop stimuli while performing either cued walking or the PSI task simultaneously. We expect both the PSI and Stroop tasks to pose inhibitory requirements, which would be manifested by deteriorated performance in response to incongruent stimuli compared to

congruent, as only incongruent stimuli required inhibition. Furthermore, we expect the two tasks to use shared resources, which should result in task interference, and we expect OA to show deteriorated performance when inhibition is required. Finally, if task interference is present, we hypothesize that OA would prioritize the PSI task, lending support to the "posture-first strategy".

Methods

Subjects

Twelve healthy YA (mean age 23±2.4 years, range 21-30 years, 5 women) and twelve healthy OA (mean age 72±3.8 years, range 66-78 years, 5 women) participated in this study. The healthy elderly were recruited locally. Subjects had no problems with their musculoskeletal system, had good eye vision and were not color blind. Older subjects had no cognitive impairments (MMSE score > 27). The experiment was approved by the local ethical committee and performed according to the declaration of Helsinki. All subjects gave their informed consent prior to participating in the study.

Precision step inhibition task

The experimental setup is illustrated in Figure 3.1 and previously described in detail [101].

Subjects walked on the C-Mill (ForceLink, Culemburg, the Netherlands) at a constant speed of 0.83 m/s. This system, comprising a software package and an instrumented treadmill, is able to project patches of light onto the treadmill relative to the subjects' foot placement, based on center of pressure patterns. These patches of light served as stepping stones and subjects were instructed to walk by stepping on the stones, unless a stone suddenly changed color during approach. In this case it was to be considered an obstacle and to be avoided by either shortening or lengthening the step. To do so, subjects needed to inhibit their ongoing step aimed at the stepping stone and find an alternative foot landing position. Stepping on or to the side of the obstacle was considered a failure. Distance between the stepping stones (i.e. step length) was individually adjusted to be comfortable and was held constant during the experiment.

The occurrence of color changing stones was random and their position was defined by the available response distance (ARD), the distance between subject's center of pressure and a virtual threshold in front of the subject (Figure 3.1c). The first stepping stone ahead of this threshold changed color, i.e. the stepping stone that was about to change color could be situated just behind this virtual threshold or at an additional distance, corresponding to the distance between the virtual threshold

and the position of the next stepping stone. Therefore, the minimal distance to the stepping stone that was about to change color was ARD, while the maximal possible distance could be “ARD + step length”. ARD was used to manipulate task difficulty. As ARD decreased, the task became more difficult because less time was available to inhibit a previously initiated step aimed at the target, and to find an alternative. However, depending on individual step length, for any given ARD the phase of the step cycle at which the stepping stone changed color could differ. The largest between-subject difference in average step length was 10 cm in OA and 8 cm in YA, meaning that, given the speed of 0.83 m/s and a step cycle of 1 s, there could be a change of about 12% and 10% of the step cycle for any given ARD condition in OA and YA, respectively. Table 3.1 shows data on step lengths. Given that our subjects walked at a constant speed of 0.83 m/s it is possible to calculate the time equivalent corresponding to each ARD by dividing ARD by the treadmill speed as *ART (ms) = ARD (mm)* / 0.83. ART values corresponding to ARD values used in our experiment are shown in Table 3.2. However, one should keep in mind that this ART definition differs from other obstacle avoidance experiments [5, 9, 10, 64, 65], who used kinematic data of the foot as a reference point, and was not manipulated directly, but rather the distance from the subject’s center of pressure to the obstacle (i.e. ARD).

Table 3.1. Average step lengths and individually determined „easiest“ level ARD values for OA and YA. Step lengths were calculated from recorded reflective marker data as half of the distance between two consecutive left heel strikes and averaged for each subject. The data for YA have been reported in [101].

	average	**SD**	**min**	**max**
step length [m]				
OA	0.48	0.03	0.43	0.53
YA	0.53	0.02	0.50	0.58
"easiest" ARD [mm]				
OA	654.55	15.08	650	700
YA	**520.83**	**51.87**	**450**	**600**

Table 3.2. Conversion between the available response distance (ARD) and available response time (ART). The ART corresponding to each ARD is calculated as *ART (ms) = ARD (mm)* / 0.83, as our subjects walked at a constant speed of 0.83 m/s. It should be noted that the technical setup manipulated ARD and allowed for variability in the precise position of the stepping stone at the instant of color change. ARD defined the minimal distance from the subject’s center of pressure to the stepping stone that was about to change color, while the maximal possible distance could be ‘ARD + step length’. Therefore, the actual ARDs could be slightly longer, depending on the subject’s step length.

ARD (mm)	**300**	**350**	**400**	**450**	**500**	**550**	**600**	**650**	**700**
ART (ms)	**360**	**420**	**480**	**540**	**600**	**660**	**720**	**780**	**840**

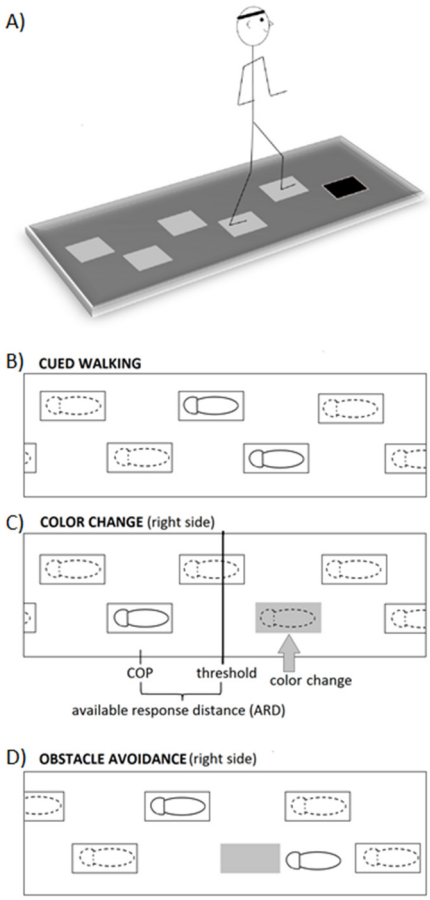

Figure 3.1. Experimental setup and conditions. Subjects walked on a system comprising a projector and an instrumented treadmill with stepping stones projected relative to subjects' gait (a). Subjects were instructed to walk by stepping on the stones (b), unless a stone changed color during approach (c). In the latter case the stepping stone represented an obstacle and subjects were instructed to avoid by either shortening or lengthening their step (d). The timing of color changes was random and the position of the stone to color was defined by the available response distance (ARD). ARD was defined as the distance between subject's center of pressure and a virtual threshold in front of the subject (c) and the first stepping stone ahead of this threshold changed color. With permission, reprinted from [101].

Experimental protocol

We followed the experimental protocol described in Potocanac et al. [101] and determined ARDs considered "easiest" individually after gradual introduction and practice of the task. Once familiar with the task the "easiest" level of difficulty was determined by performing short versions of the task starting from a difficulty level at which all subjects were expected to be able to perform the PSI task (as based on a pilot study; OA ARD = 700 mm, YA ARD = 600 mm). Three obstacles were presented at this task difficulty and, if avoided successfully, task difficulty was increased (by decreasing the ARD by 50 mm) until the subject's first failure. This procedure was performed twice and the mean value of ARDs at which the failures occurred was used as "easiest" level for the main experiment.

The protocol consisted of a baseline walking task condition (cued walking without obstacles) followed by 4 conditions with increasing difficulty. The individually

determined “easiest” level was used for the starting condition and for the subsequent conditions the ARD was decreased each time by 50 mm. Each condition consisted of 20 obstacles that could appear at either foot, at a frequency of 7 per minute. After a break, subjects repeated the same PSI task conditions with an auditory DT. Cued walking without any obstacles was used as a baseline for Stroop task performance. Participants were instructed to perform both the PSI and the Stroop tasks to the best of their abilities.

Auditory dual (Stroop) task

The auditory DT stimuli consisted of words “high” and “low”, spoken in a high or low pitched voice. The stimuli were either congruent (spoken word matched the pitch used) or incongruent (the word did not match the pitch) and subjects had to respond as fast as possible by verbalizing the pitch. The stimuli were presented continuously, randomized, with the interstimulus interval set to approximately 1.2 s. Subjects’ responses were recorded wirelessly.

Data analysis

We verified failures on the PSI task by video recordings of the experiment. Failure rates were calculated by dividing the number of failures by the total number of obstacles presented. Performance of OA on the PSI task was compared to previously reported performance of YA [101].

The Stroop task resulted in several hundred responses per condition. Therefore, a computerized analysis program was devised that extracted and recognized the spoken words, based on the Mel-frequency cepstrum coefficients matched to previously created Gaussian mixture models of words “high” and “low”. The accuracy of the word recognition, as evaluated by 10-fold cross validation of the learning set consisting of 703 sounds, was 93.5%. The pitch analysis based on Subharmonic-to-Harmonic Ratio [114] resulted in 100% accuracy. Responses could be either correct, incorrect (i.e., wrong reply given) or omitted (i.e., no reply given). Response latency was defined as time between the stimulus offset and the response onset. Latencies of correct responses and rates of correct, incorrect and omitted responses were analyzed for congruent and incongruent stimuli separately. This allowed for a detailed evaluation of performance: as performance deteriorates one first takes longer to respond correctly, makes more incorrect responses, and eventually might stop responding altogether. Furthermore, since good performance on the Stroop task means both accurate and fast responses, a composite score combining speed and accuracy was calculated as a ratio of the rate of correct responses (%) and average latency of correct responses (s) [10]. This composite score enables easy assessment of the overall Stroop performance and was calculated for incongruent and congruent stimuli in each PSI task condition. Analyses were

performed using VOICEBOX toolbox [115] and MATLAB 2011b (Mathworks, Natick, MA, USA).

Due to technical problems, two YA did not perform the DT and the Stroop task data of one YA and PSI task data of one OA were unavailable.

Statistical analysis

PSI task failures were analyzed using a 2 (age) x 4 (difficulty conditions) x 2 (single task (ST) vs. DT) repeated measures ANOVA procedure, followed by a Tukey HSD post-hoc test. Additionally, individually determined "easiest" level ARDs and failure rates were compared between the groups using a Mann-Whitney U test. Stroop task performance (composite score, latencies of correct responses and rates of correct, incorrect and omitted responses) was analyzed using a 2 (age) x 5 (baseline and 4 difficulty conditions) x 2 (congruence) repeated measures ANOVA procedure, followed by a Tukey HSD post-hoc test. Analyses were performed using Statistica 10 (StatSoft, Tulsa, OK, USA) with level of statistical significance set at $\alpha = 0.05$.

Results

Precision step inhibition task performance

On average, the "easiest" level ARD was 655±15 mm (range 650 – 700 mm) in OA, while in the YA this was 521±54 mm (range 450 – 600 mm). These ARD values correspond to average ARTs of 786±18 ms (range 780 – 840 ms) in OA and 625±65 ms (range 540 – 720 ms) in YA. Mann-Whitney U test showed a statistically significant difference in "easiest" level ARD between age groups ($p < 0.001$). Figure 3.2 clearly shows that the range over which the two groups could be tested differed, although there was some overlap. This difference in range was due to the older subjects starting to fail sooner than the YA during the process of determining individual "easiest" ARD level. Poor performance of OA was also reflected in higher failure rates of OA compared to YA in the "easiest" condition, for both ST ($p = 0.005$) and DT ($p = 0.006$). In OA these rates were on average 40±22% (range 15% – 80%) for the ST and 45±12% (range 30% – 60%) for the DT, while in YA these were 16±11% (range 5% – 35%) for the ST and 27±11% (range 15% – 45%) for the DT. Finally, for the range of overlapping ARDs, OA had higher failure rates than YA. Adding a DT increased failure rates in all conditions for both age groups.

Although most subjects had an increase in failure rates with increasing PSI task difficulty there were some subjects in the OA group that showed improvement in task performance over time, resulting in no significant main effect of age for the repeated measures ANOVA. We did find significant main effects of task ($p = 0.002$) and difficulty ($p < 0.001$) and an interaction of age and difficulty ($p < 0.001$). Failure

rates were higher when the PSI task was performed under DT conditions and as ARD decreased. However, the difficulty effects were driven by YA and not significant in the group of OA alone.

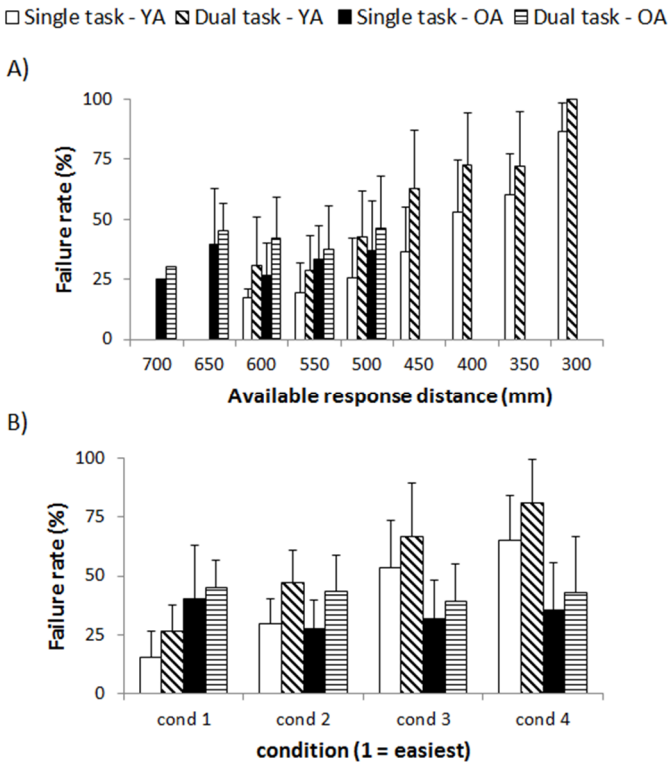

Figure 3.2. Average failure rates per individually determined available response distances (2a) and conditions (2b), for OA and YA. Lower available response distances indicate higher task difficulty. Condition 1 is the easiest and the difficulty is increasing in subsequent conditions. Error bars denote standard deviations. See text (section 'Precision step inhibition task performance') for statistical details.

Stroop task performance

Composite scores

Composite score data are shown in Figure 3.3. Repeated measures ANOVA showed significant main effects of age ($p = 0.03$), indicating deteriorated performance of OA, and PSI task difficulty ($p < 0.001$), indicating worse performance during PSI compared to baseline cued walking ($p < 0.004$ for each of the difficulty conditions). A significant main effect of congruence ($p < 0.001$) indicated performance was generally lower for incongruent stimuli, but a significant interaction of age and congruence ($p = 0.02$)

indicated that only OA performed significantly worse in response to incongruent stimuli compared to congruent ($p < 0.001$). Additionally, age resulted in deteriorated performance only in response to incongruent stimuli, when OA performed significantly worse than YA ($p \leq 0.01$). Combining these two results shows that OA and YA performed equally well in response to the congruent stimuli and only the performance of OA deteriorated when stimuli became incongruent.

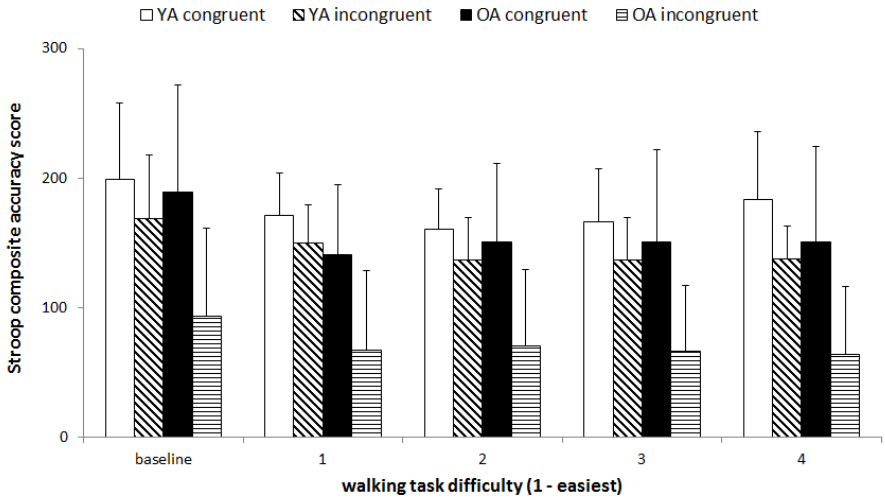

Figure 3.3. Stroop composite scores, combining speed and accuracy of responses, for congruent and incongruent stimuli for OA and YA. This score is calculated as rate of correct responses (%) divided by average latency of correct responses (s). A low score indicates poor performance. Error bars denote standard deviations. See text (section 'Composite scores') for statistical details.

Rates of correct responses

Average rates of correct responses during baseline walking were 83.2±16.4% and 81.6±16.2% in YA and 78.1 ±18.1% and 52.4±32.8% in OA, for congruent and incongruent stimuli respectively (Figure 3.4a). Repeated measures ANOVA showed significant main effects of age (OA performed worse than YA, $p = 0.003$), PSI task difficulty (performance on the PSI task deteriorated compared to baseline cued walking, $p = 0.004$), congruence (performance deteriorated in response to incongruent stimuli, $p = 0.001$) and interaction of age and congruence ($p = 0.01$). OA performed worse than YA in response to incongruent stimuli ($p < 0.001$), but equally well when stimuli were congruent.

Rates of incorrect responses

In line with correct responses, OA showed, on average, higher rates of incorrect responses than YA (Figure 3.4b), both in response to congruent and incongruent stimuli (congruent YA = 5.4±8.4%, OA = 8.6 ±6.4%; incongruent YA = 5.3±5.7%, OA = 31.3±25.2%). Repeated measures ANOVA showed significant main effects of age ($p = 0.01$), congruence ($p = 0.004$) and significant interaction effects of age and congruence ($p = 0.01$), PSI task difficulty and congruence ($p < 0.001$), and PSI task difficulty, age and congruence ($p < 0.001$). Rates of incorrect responses were higher in OA and for responses to incongruent stimuli. OA performed worse than YA in response to incongruent stimuli ($p = 0.004$), but equally well when stimuli were congruent. The congruence effect was only significant in OA, who performed worse in response to incongruent stimuli as compared to congruent ($p = 0.002$). PSI task difficulty x congruence interaction was such that the congruence effects were significant when obstacles were included in the PSI task (all difficulty levels, $p \leq 0.008$), but not during baseline walking. Finally, significant results for the three way interaction showed that only the performance of OA in response to congruent and incongruent stimuli differed already during baseline cued walking ($p = 0.017$).

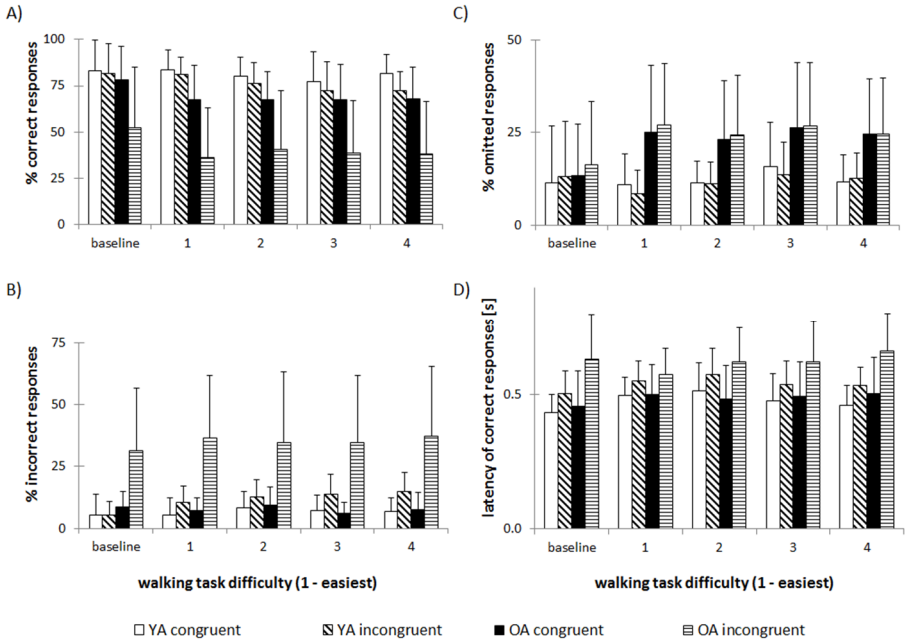

Figure 3.4. Performance on the auditory Stroop task. Rates of correct (4a), incorrect (4b) and omitted responses (4c) and latencies of correct responses (4d) are shown for responses to congruent and incongruent stimuli separately for OA and YA. Error bars denote standard deviations. See text (section 'Stroop task performance') for statistical details.

Rates of omitted responses

Rates of omitted responses during baseline walking were 11.5±15.3% and 13.1±14.9% in YA and 13.3±14.0% and 16.3±17.1% in OA for congruent and incongruent stimuli, respectively (Figure 3.4c). When obstacles were added to baseline cued walking these rates were 10.9±8.2% and 8.5±6.2% in YA and 25.2±18.0% and 27.0±16.5% in OA for congruent and incongruent stimuli, respectively. We found a significant interaction between age and PSI task difficulty ($p = 0.04$), indicating OA omitted significantly more responses than YA for the two most difficult PSI task conditions, compared to baseline cued walking.

Latencies of correct responses

Finally, for the response latencies (Figure 3.4d), we found a significant main effect of congruence ($p < 0.001$) and interaction effects of age and congruence ($p = 0.001$) and of PSI task difficulty and congruence ($p = 0.04$). Both age groups showed longer latencies for correct responses in response to incongruent compared to congruent stimuli (both $p < 0.001$). On average, the YA showed shorter latencies than OA, both in response to congruent and incongruent stimuli (baseline walking: congruent YA = 0.43±0.07 s, OA = 0.46 ±0.13 s; incongruent YA = 0.50±0.09 s, OA = 0.63±0.17 s). OA's responses to incongruent stimuli took significantly longer than responses of YA to congruent stimuli ($p = 0.03$). PSI task difficulty did not affect responses to incongruent stimuli, but it did influence the latencies of correct responses to congruent stimuli, which were longer for the two easiest difficulty levels compared to baseline cued walking ($p < 0.025$).

Discussion

In the first part of the discussion we focus on PSI task performance of both groups, analyzing task difficulty and failure rates. The second part of the discussion focuses on performance under DT conditions. Performance of OA and YA on the Stroop task and the interference between the two tasks are discussed with respect to the inhibitory requirements of the two tasks, subjects' abilities, and task prioritization.

Performance on the precision step inhibition task

The main aim of this paper was to explore whether OA could be tested using our novel PSI task that evaluates response inhibition by requiring adjustments of ongoing, precisely aimed steps. OA successfully performed the PSI task at different, individually adjusted difficulty levels, however their performance was worse than previously reported performance of YA [101]. This was evident by higher failure rates at both individually adjusted "easiest" ARD levels (which differed, but were performed after equal amounts of practice in both groups) and for overlapping ARD levels (which reflect absolute task difficulty).

In general, this increased failure rate is in line with age related decline in inhibitory abilities measured in a hand test of response inhibition [22] and consistent with previous experiments showing deteriorated ability of older adults to initiate fast voluntary steps [39] and modify desired foot landing positions [7]. Furthermore, our data are in line with previous obstacle avoidance experiments showing deteriorated ability of older adults to avoid physical [5, 10] and virtual obstacles [64, 65]. However, some results from the present study differed from previous obstacle avoidance studies, probably because our PSI task stressed inhibition, as our subjects initially aimed to step onto stepping stones turning into virtual obstacles (while previous work did not require precision stepping). In particular, previous experiments on obstacle avoidance found that OA of comparable age had success rates over 90% with ARTs over 350 ms for avoidance of physical obstacles [5, 10] and 450 ms for avoidance of virtual obstacles [64, 65]. In contrast, in our setup, OA needed more time and had failure rates of 40.5% for ARDs of 654.5 mm (equivalent of 785.5 ms at a treadmill speed of 0.83 m/s). This finding was in line with our previously reported data of YA [101], and confirms that performing the PSI task requires more time. This could be related to increased task complexity, as obstacles are presented on both sides, consistent with previous data showing a significant delay in onset of reactions to suddenly appearing obstacles when switching from a one sided to a two sided paradigm [59]. Additionally, it is possible that in previous experiments [5, 10] subjects fixated their gaze on the obstacle prior to its release, while in our case they did not know where the stepping stone turning into an obstacle would be positioned. However, some of the differences in timing could also be caused by the differences in the technical setup. In our experiment the distance from the subjects' center of pressure to the stepping stone to change color was manipulated, and not ART directly. Furthermore, the differences in subjects' step lengths could cause variability in the phase of the gait cycle in which an obstacle was presented of about 10%-12% for any given ARD, which could account for about 100 ms of the additional time needed for successful obstacle avoidance.

Inhibitory requirements and abilities

The second aim of this paper was to assess inhibitory requirements of the two tasks, the potential use of shared inhibitory resources and a possible age related decline in inhibitory abilities. We hypothesized both tasks would require inhibition, thus causing interference effects and providing evidence that both tasks tapped into the same pool of global response inhibition. Furthermore, we expected deteriorated performance in the group of OA.

The Stroop task in itself requires motor inhibition with respect to the act of speaking. To give a correct response to incongruent stimuli, one needs to inhibit the processing of irrelevant information. Therefore, similar to work of Redfern et al. [49], the difference in performance between congruent and incongruent Stroop stimuli can

indicate inhibition abilities while controlling for the listening and speaking elements of the Stroop task. Although some studies reported no significant effect of congruence during obstacle avoidance [109, 116], we found the rates of correct responses to incongruent stimuli to be lower than when responding to congruent stimuli (on average about 4% in YA and 28% in OA). These findings are in line with previous reports of incongruent auditory Stroop stimuli during obstacle avoidance resulting in a decreased composite score consisting of accuracy and latency measures [10] and show that the performance deteriorates when inhibition is required, i.e., in response to incongruent Stroop stimuli. The importance of inhibition for successful execution of these tasks is further supported by the fact that congruence affected the rate of incorrect responses in YA only when obstacles were added to baseline cued walking, indicating that the additional inhibitory requirements are indeed related to obstacle avoidance and not just dual tasking (i.e., cued walking, listening and talking). In addition, interference between the two tasks requiring response inhibition, supports the notion of a "global" mechanism of response inhibition when speed is essential [28, 110].

Finally, in line with previous findings indicating that inhibitory abilities deteriorate with increasing age [98, 99], we found that OA performed worse than YA only when the Stroop task required inhibition, i.e. when responding to incongruent Stroop stimuli. OA performed as well as YA in response to congruent Stroop stimuli, which required no inhibition.

Task prioritization

When combining PSI with the Stroop task, OA's performance on the PSI task did not deteriorate, but they did perform worse on the Stroop task, which indicates that older subjects prefer a "posture first" strategy under the present conditions. This is in line with previous studies reporting that OA prioritize stability when it is threatened [111, 112]. In contrast, Hegeman et al. [10] reported diminished obstacle avoidance performance in a group of OA when using an auditory Stroop task in combination with obstacle avoidance during treadmill walking. This apparent discrepancy might be due to several elements. Firstly, the PSI task was more difficult, thereby requiring potentially more cognitive resources in itself [103]. Secondly, there was an age difference between the experimental groups in these two studies. Average age of OA in our study was 72 years (range 66-78 years), while Hegeman's subjects were on average 60 years old. It has been previously suggested that the decline in performance during obstacle avoidance occurs at about 70 years of age [5]. It is possible that the stability of our subjects was threatened more and therefore needed to be prioritized.

In contrast to OA, in YA the addition of the Stroop task significantly increased failure rates on the PSI task (on average by 14.6%). This is in line with a study by

Weerdesteyn et al. [57], who reported a failure rate increase of 11% during obstacle avoidance with a Stroop DT [57]. In contrast others [109, 117] did not see an effect of the DT on obstacle avoidance success rates in YA and attributed this to prioritization of the walking task. Apparently, in our case, the YA did not prioritize the PSI task, as indicated by the bidirectional interference between the two tasks. A possible explanation lies in the fact that both of our tasks were more demanding and therefore perhaps more prone to DT interference. We used a continuous Stroop task, with stimuli presented every 1.2 s on average, while Siu et al. [109] used a single Stroop stimulus per walking trial and Brown et al. [117] used a verbal reaction time task. Furthermore, we used precision stepping under time pressure on a treadmill, while others [109, 117] used overground walking. All these differences help explain why the Stroop task performance was also affected by DT interference. More generally it is clear that the issue of prioritization depends heavily on task difficulty. This lends support to the proposals that prioritization is a dynamic process [118] that "is likely to be ruled by a controlled/automatic ratio that is imposed by the difficulty of the tasks rather than a prioritization framework" [103].

Limitations

Due to the frustration and discouragement observed when subjects were not able to perform the task at given ARDs during pilot experiments, we used an experimental protocol with increasing PSI task difficulty, which was individually adjusted based on initial ability. In principle, the sequential experimental design could have resulted in fatigue effects (leading to more failures in the more difficult conditions later on). This clearly was not the case in OA, and was checked for and not seen in YA [101]. However, a side effect of the sequential presentation was that a learning effect appeared in OA (see Figure 3.2b, conditions 1 and 2). It seems that, although they initially performed very poorly, with more training our OA might be able to perform the PSI task at more difficult levels, perhaps even comparable to the YA. This was in hindsight a major limitation, as the protocol we followed worked very well in determining the ARDs at which YA show a dramatic increase of failures, from 15.5% in the ST to a maximum of 80.8% during DT [101]. Because of this learning effect we cannot address the magnitude of age related deterioration in PSI task performance. However, we interpreted our data with due caution and believe the learning effect does not affect the proposed conclusions. Future research could possibly use constant ARD values in order to address this issue (although determining ARD values that could be used for all subjects in both groups will be a challenge).

Secondly, in our experiment the Stroop task stimuli were presented continuously, but were not synchronized to the obstacle presentation in the PSI task. Given the number of Stroop stimuli (several hundred per condition) and the fact that congruent and incongruent stimuli were randomized and counterbalanced, we believe this has no effect on our results. Future research could benefit from

synchronizing the Stroop stimuli to obstacle presentation (see e.g. [10], as this would enable assessment of possible congruence effects on different phases of the precision step inhibition.

Conclusions

OA were able to perform the PSI walking task, but their performance was worse than previously reported performance of YA. The combination of PSI and Stroop tasks was successful in eliciting DT interference in both YA and OA, probably because it was more demanding than previously used tasks. This DT interference confirmed that the PSI walking task stressed inhibitory requirements in YA, as the Stroop task, when requiring inhibition, affected the rate of incorrect responses during the PSI task, but not during baseline cued walking. Furthermore, Stroop task performance confirmed that OA have difficulties with inhibition, which is in line with experiments on hand function. Finally, we can conclude that OA are able to inhibit their responses on both tasks, but that, unlike YA, they prefer a "posture first strategy" when combining a PSI motor task with a DT.

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4 QUICK FOOT PLACEMENT ADJUSTMENTS DURING GAIT: DIRECTION MATTERS

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Abstract

To prevent falls, adjustment of foot placement is a frequently used technique to regulate and restore gait stability. While foot trajectory adjustments have been studied during step initiation, online corrections during walking are more common in daily life. Here, we studied quick foot placement adjustments during gait, using an instrumented treadmill equipped with a projector, which allowed us to project virtual stepping stones. This allowed us to shift some of the approaching stepping stones in a chosen direction at a given moment, such that participants were forced to adapt their step in that specific direction and had varying time available to do so. Thirteen healthy participants performed six experimental trials all consisting of 580 stepping stones and 96 of those stones were shifted anterior, posterior or lateral at one out of four distances from the participant. Overall, long step gait adjustments were performed more successfully than short step and side step gait adjustments. We showed that the ability to execute movement adjustments depends on the direction of the trajectory adjustment. Our findings suggest that choosing different leg movement adjustments for obstacle avoidance comes with different risks and that strategy choice does not depend exclusively on environmental constrains. The used obstacle avoidance strategy choice might be a trade-off between the environmental factors (i.e., the cost of a specific adjustment) and individuals' ability to execute a specific adjustment with success (i.e., the associated execution risk).

Keywords

Falls, locomotion, obstacle avoidance, online corrections, stepping accuracy, walking

Introduction

Fast online corrections have been studied widely for arm movements using a double-step paradigm (reaching to a target that is shifted during the reach). The resulting corrective movements can have a latency that is shorter than the reaction time for voluntary movements [119–121], which has led to the suggestion that these corrective movements are mediated subcortically [19]. However, a fast pathway over the parietal cortex remains an option as well [122–124].

More recently, similar experiments have been performed for leg movements. For example, in some experiments the participants performed a task involving step initiation onto an illuminated target that sometimes moved to left or right during the stepping movement, requiring a foot trajectory adjustment (e.g. [7, 52, 125]. These authors found that leg movement adjustments were also fast and could "occur at much shorter latency than conventional visuomotor reaction tasks" [125]. Again, the suggestion was made that subcortical mechanisms could be involved (see also [58]).

In daily life such fast adjustments need to be made often while walking and not just during step initiation [126]. Hence there is a need for experiments about online corrections during gait. Such experiments come close to those performed by Moraes et al [66]. In these experiments the participants were asked to walk on level ground and avoid stepping on a virtual white planar obstacle, when present. They had one-step duration to adjust the step in order to avoid the obstacle and had to do it in the cued direction (an arrow projected over the white planar obstacle cued the alternate foot placement). The authors could link preferred alternate foot placement strategies in unconstrained conditions to success rates of alternate foot placement in cued conditions. Long steps (over the obstacle) were preferred over short steps (in front of the obstacle) and they were performed more successfully. Similarly lateral side steps were preferred over medial side steps and they were performed more successfully [66]. However, adjustments in the plane of progression were not directly compared with lateral step adjustments and the effects of time pressure were not evaluated (conditions were compared at constant time constraints using overground walking which allowed for slowing down). Finally, these experiments differed from the dual-step ones described above in that that there was no target shift, but rather the projection of a virtual obstacle along with a cue.

A closer approximation of the dual-step paradigm was achieved by Young and Hollands [8]. Participants were asked to walk towards, and step accurately onto, a visual target which, during the step towards it, moved to an unpredictable location at an unpredictable time. Older individuals characterized as having high risk of falling produced significant deviations in foot trajectory with latencies that were longer compared to those obtained by low-risk older adults. While very relevant, this

paradigm does not easily allow manipulating time pressure systematically, as can be done with treadmill experiments [58].

In the present study we used a dual-step paradigm during walking on a treadmill with targets that could shift either in the sagittal or in the frontal plane. The aim was to address the role of temporal constraints on cued gait adjustments and to directly compare adjustments in the plane of progression with lateral side steps. We used an instrumented treadmill equipped with a projector which allowed us to project stepping stones according to the participants' gait [101, 127, 128]. This also allowed us to shift some of the approaching stepping stones in a chosen direction at a given moment, such that participants were forced to adapt their step in that specific direction and had varying time available to do so.

As mentioned, these experiments on dual-steps under time pressure are comparable to experiments on avoidance of obstacles, either real [9] or virtual [6, 68]. From some of these experiments it is known that time pressure can affect the choices of avoidance strategy. For example, a step lengthening strategy (long step strategy, LSS) is typically used when time pressure is low, but step shortening (short step strategy, SSS) is preferred when the available response time is short (see e.g. [5]). One can assume that this occurs because people can make long steps more accurately than short steps, but this could not be tested in these experiments. In contrast, the present experiment allows evaluating the accuracy of stepping since one can calculate the deviations of the landing position with respect to the shifted target. Based on the assumption that long steps are preferred because of precision it was expected that long step gait adjustments in cued conditions would be more accurate and successful than short steps under time pressure.

Methods

Participants

We recruited 13 healthy participants (ages 20 – 28), who had no known history of neurological disorders, musculoskeletal problems or vision impairments. All participants reported right foot dominance. The experimental protocol was approved by the local ethics committee in accordance with the guidelines of the Declaration of Helsinki. Informed consent was obtained from all individual participants included in the study.

Procedures

We used an instrumented treadmill equipped with a projector and C-mill software (Motekforce Link, Culemborg, the Netherlands) to project stepping stones according to the participants' gait [101, 128, 129]. After a treadmill walking familiarization

period of five minutes at 3.6 km/h, we recorded ground reaction forces during 20 strides of the participants' natural gait, while no stepping stones were projected. Based on these ground reaction forces (recorded at 1000 samples/second), center of pressure trajectories were generated and foot-strike events, toe-off events and step lengths were extracted using the center of pressure trajectories [127]. For each participant the average step length over the recorded strides, foot width and length were measured and used to generate eight individualized stepping stone sequences: two familiarization and six experimental sequences. All stepping stone sequences had the same structure of stepping stones: anterior-posterior center to center distance of the stepping stones was equal to the participants' step length, while the medio-lateral center to center distance was 0.2 m for all participants since this was observed to be a comfortable distance in pilot experiments (Figure 4.1). All six experimental sequences were different (as explained below), but it should be noted that they did not differ between participants, except for step length and stone size (see above).

For the remainder of the experiment stepping stones were projected on the treadmill's surface and participants were instructed to walk by stepping on the projected stepping stones, approaching the participant at a velocity equal to the belt speed (3.6 km/h). In addition, each stepping stone could be shifted to a predefined new position at the moment that the stones came within a predefined distance from the participant's center of pressure (the "available response distance"; ARD) [101]. Stepping stones were shifted either in the plane of progression (away from; 'long step', or towards the participant; 'short step') or laterally ('side step'; Figure 4.1). Some pilot experiments were used to determine the optimum displacements to be used in the main experiments. The displacement of the stepping stones was 40% of the average step length (Figure 4.1) for stepping stones shifted in the plane of progression and 20% of the average step length for stepping stones shifted laterally. Furthermore, we used ARDs of 0.4, 0.5, 0.6 and 0.7 m, to evaluate the effect of time available on gait adjustment performance.

The first familiarization sequence consisted of 20 non-shifting stepping stones and was performed once, without recording. The second familiarization sequence was similar to the first, but stepping stones #6, #11 and #16 were shifted while approaching (long step, short step and side step, respectively; ARD: 0.7 m for all). The six experimental sequences all consisted of 580 stepping stones and 96 of those stones were shifted. In each experimental sequence all ARDs were equally represented (each 24 times). Stepping stones to shift were selected pseudo randomly and were interleaved with a random number (4-7) of normal, non-shifting stepping stones, to give the participant time to recover after a possible loss of balance. The participants were not able to predict which steps would be shifted. To be able to evaluate possible anticipation effects the sequences were divided into two

groups. In one group, the “single direction trials”, all shifted stones within a trial were shifted in the same direction, requiring either long, short or side steps, depending on the trial. In contrast, in the three mixed direction trials, within each sequence the stones shifted randomly in one of three directions. In total there were 24 perturbation conditions (2 anticipation conditions (single/mixed) × 3 directions (long/short/side) × 4 ARDs). The six experimental sequences were presented in random order to prevent any confounding effects of learning or fatigue.

In addition to the moving stepping stones, we projected a stationary walking area (1.25m long, covering the treadmill width) that served as a cue for the participants to keep their position on the treadmill, preventing them from slowing down and reaching the back end of the treadmill. The participants were told in advance whether they were about to perform the “single direction” trials. We instructed the participants to place their feet in the center of the stepping stones to their best ability. In addition, we informed them that sometimes this would not be possible due to the high time pressure. During the trials the ground reaction forces were recorded at 1000 samples/second.

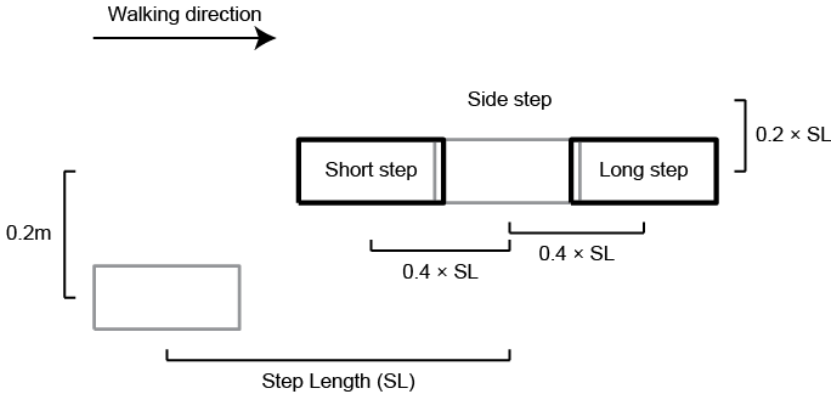

Figure 4.1. Approaching stepping stones could be shifted, cueing the participant to make a long step, short step or side step. Long steps were shifted away from the participant by 40% of the average step length; short steps were shifted the same distance towards the participant. For the side steps the displacement was set 20% of the average step length and was always lateral (stepping stones for the left foot shifted to the left side and stones for the right foot to the right).

Data analysis

For each step we established the COP location during mid-stance (at 50% of the time between heel strike and toe-off) and matched these to the stepping stones. Then, we analyzed all stepping stones that were shifted and used the non-shifting stepping

stones 2 and 3 steps ahead of those as baseline. For each experimental trial we calculated the mean offset distance between the baseline stepping stones and the accompanying mid-stance COP locations. For each shifted stepping stone we calculated the same distance and corrected this for the baseline offset to obtain a measure of foot placement error. For the forward and backward shifted stepping stones we evaluated the anterior-posterior distance; for the sideward shifted stones we evaluated the medio-lateral distance. In addition we used the borders of the stepping stones (which equaled the foot length and width) as a criterion for successful step adjustment. All steps for which the corrected COP location was within the outline of the stepping stone were considered successful. Then we calculated success rates for each of the 24 perturbation conditions by dividing the number of successful steps by the total number of steps in each condition.

Statistics

Wilcoxon signed rank tests were used to compare success rate between legs (preferred vs. non-preferred) and success rates between anticipation conditions (single vs. mixed). The data of single and mixed trials were then collapsed and Friedman ANOVA was used to analyze success rates between the 3 directions and between the 4 ARDs. Wilcoxon signed rank test with appropriate Bonferroni correction was used for post hoc testing. Level of statistical significance was set to $\alpha < 0.05$.

Results

The participants walked with a step length of 0.55 ± 0.04m (mean ± SD). Participants were well able to walk on the track of projected stepping stones, but when the stepping stones shifted at small ARDs, participants failed to change landing position and usually placed their feet close to where the stepping stone would have been if the shift would not have occurred (Figure 4.2, left panel; data for a typical participant).

With larger ARDs, participants were increasingly more successful in placing their feet in the new location of the stepping stone (Figure 4.2, right panel; data for a typical participant). Overall, success rates were higher for the preferred leg than for the non-preferred leg (44 ± 12% vs. 37 ± 10%; $p = 0.0007$). Success rates from the single direction trials were similar to those from the mixed direction trials ($p = 0.45$). Overall, long step gait adjustments were performed more successfully (51 ± 32%) than short step (29 ± 25%; $p = 0.0002$) and side step gait adjustments (42 ± 29%; $p = 0.0012$), while the latter two were performed equally successfully ($p = 0.14$). To assess whether time pressure had a different effect on step lengthening, shortening or side stepping, we compared the three directions at different ARDs. For each of the four ARDs a main effect of direction was observed (Table 4.1). Long step gait

adjustments were performed more successfully than the short step gait adjustments at all ARDs and were more successful than side steps at an ARD of 0.5m ($p < 0.05$). At the other ARDs the latter difference did not survive the Bonferroni correction. Short steps and side steps were equally successful (Figure 4.3; Table 4.1).

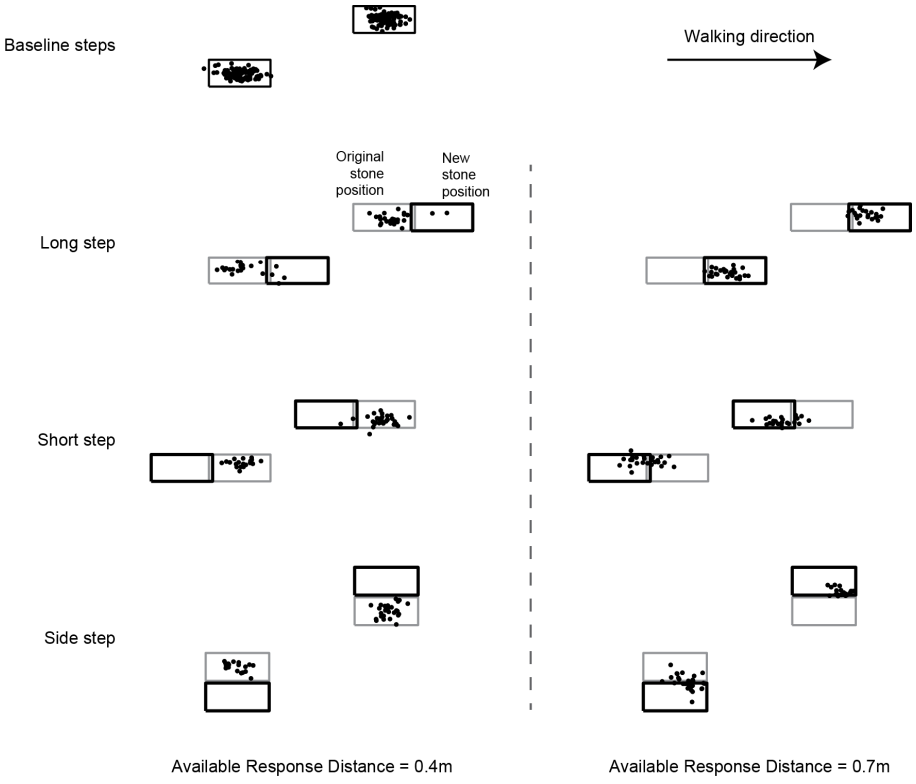

Figure 4.2. Foot placement locations relative to the stepping stones for baseline steps and shifted stepping stones for a typical participant. This participant was clearly more successful when the available response distance was large (right panel; many steps inside the outline of the new location), than when the available response distance was small (left panel; many steps outside the outline of the new location and inside the outline of the original location). Furthermore, long steps were more successful than short steps and side steps for both available response distances.

Table 4.1. Significant direction main effects can be observed for all available response distances (ARD).

	Criterion	***ARD 0.4m***	***ARD 0.5m***	***ARD 0.6m***	***ARD 0.7m***
Main effect	$p < 0.05$	0.049*	0.023*	0.005*	0.001*
Long vs Short	$p < 0.017$	0.010*	0.010*	0.002*	0.001*
Long vs Side	$p < 0.017$	0.019	0.002*	0.021	0.052
Short vs Side	$p < 0.017$	0.332	0.367	0.094	0.022

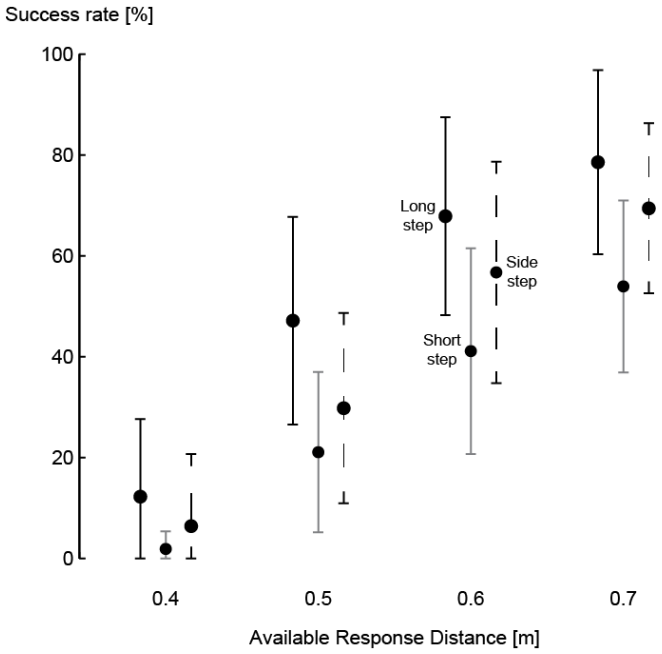

Figure 4.3. Long step gait adjustments have the highest success rates. Success rates increase with increasing available response distance. For all available response distances the long step gait adjustments have higher success rates than short step gait adjustments. Error bars represent ± 1 SD.

Discussion

In this study we evaluated the ability to execute gait adjustments under varying levels of time pressure, directly comparing adjustments in the plane of progression with lateral side steps. We observed that young subjects are able to make these

adjustments even when there is high time pressure. Overall, long step gait adjustments were performed more accurately and successfully than short and side step gait adjustments, thereby confirming our expectation. To our knowledge this is the first study to evaluate the ability to adjust leg movements during treadmill walking in response to a double-step paradigm, consisting of a target shift in the anterior, posterior, and lateral direction. In contrast, there are already some data available for lateral target shifts but these involve either uncued overground walking [8] or step initiation [7, 52, 53, 125]. For frontal plane adjustments, the current data complement these results by showing that fast lateral adjustments are possible, and even slightly (although not significantly) more successful than step shortening, during ongoing walking on a treadmill.

What might cause the difference in success rates?

Step lengthening might be the most successful way of adjusting leg movements in the sagittal plane because of several reasons. Firstly, it allows for more time to implement a change [9, 76]. Secondly, long steps are biomechanically more similar to a normal, unperturbed step and therefore might be easier to implement, since activation of the same muscles is required to prolong the ongoing movement. On the other hand, step shortening requires inhibition of ongoing movement and activation of antagonist muscle to rapidly lower the foot. Furthermore, stability requirements during step shortening might be a limiting factor for the ability to execute this adjustment. During step shortening the foot moves backward while the COM moves forward, creating unstable gait [130]. A study forcing prescribed directions of leg movement adjustments for obstacle avoidance during overground walking [66] reported that successful step shortening for obstacle avoidance resulted in smaller margin of dynamic stability, indicating increased instability during obstacle crossing. Additionally the margin of dynamic stability for step shortening did not return to baseline in the step following obstacle crossing, suggesting it takes longer to recover from the associated balance perturbation [66].

Relation to avoidance of obstacles

Although we studied the ability to execute gait adjustments when stepping towards a target it is interesting to relate these findings to obstacle avoidance experiments. These tasks are similar in so far that both require fast adjustment of foot trajectory based on environmental constraints, but the major difference is that obstacle avoidance studies focus on the type of adjustment which is being chosen under specific environmental condition in order to avoid an obstacle. In contrast, the present study looks at the ability to perform a specific (cued) adjustment when a target is given. One could expect that the ability to perform an adjustment might influence how often it is being chosen for obstacle avoidance. If step lengthening can

be executed more accurately than step shortening, then one can learn to use this as the preferred strategy when a choice has to be made in order to avoid an obstacle.

In this respect, our findings are in line with previous work showing that young adults prefer step lengthening over step shortening when available response time is high [6, 9, 66] and that older adults prefer step lengthening when real obstacles are concerned [9]. Comparing the failure rate with the rate of executed steps for lengthening and shortening during obstacle avoidance on a treadmill it is clear that step lengthening is performed with more success and this might be why long steps are preferred [9]. Given the disadvantages, the question arises why one still would use short steps. A possible explanation lies in the fact that long steps come at a higher metabolic cost [9] and thus using step shortening would be rewarding, if the error rate is sufficiently low.

In line with our findings, in another study, involving cueing a specific adjustment direction for avoidance of virtual obstacles during overground walking [66], the authors found highest success rates for step lengthening, followed by lateral and shortened steps. In addition, a preference for step lengthening was found in 5 out of 8 participants, although shortening the step or stepping to the side required a smaller foot displacement [66]. The authors suggested that the reason for choosing step lengthening might be due to a preference for an adjustment that minimizes threats to stability during obstacle crossing and allows for a faster return to normal walking stability. While successful step shortening is detrimental for stability, (any) unsuccessful movement adjustment resulting in obstacle contact might be even more detrimental. Our data show that the risk of failure using step shortening is clearly highest. This is in line with the data of Chen et al [6] showing that tripping occasionally occurred when subjects tried to perform a short step strategy while walking and encountering a virtual obstacle.

The role of anticipation

One of the aims of this study was to evaluate the role of anticipation on gait adjustment performance. We compared performance during single direction trials, where all shifted stones within a trial were shifted in the same direction, with mixed direction trials, where within each trial stones shifted randomly in one of three directions. In the single direction trials, participants could anticipate which gait adjustment (long, side or short step) would be required, while in the mixed direction trials such anticipation was not possible. Success rates of the single direction trials were similar to those from the mixed direction trials, indicating that even though participants were aware of which adjustment was required in the event of stone shift, they did not perform it more successfully. This finding is somewhat surprising, since one could expect the participants to be able to preplan the required foot movement and execute it more rapidly in the event of (any) change in their visual

context. Similar anticipation effects were previously reported for tripping perturbations [131]. However, it should be noted that it was always impossible to anticipate which stepping stone would be shifted and when. This may explain our result since knowledge of the direction is presumably only helpful when one is also able to anticipate when to use a preplanned movement. In fact, the lack of anticipation effects is an argument to demonstrate that the current adjustments were true online corrections, without contamination with preprogrammed reactions.

Limitations and future perspectives

In the present experiments it was not possible to measure the ability to execute medial movement adjustments since participants would risk tripping and stepping on the gap between the two belts of the dual-belt treadmill. However, the lack of medial deviations was probably not a major limitation since Moraes et al [66] found that subjects prefer lateral steps anyway. A superior ability to perform lateral steps was also observed in gait initiation experiments [7, 50] and in walkway trials [8]. In addition, it may be argued that the relevant population is not young adults but elderly or patients. Falls during gait are a significant problem in patient populations [3, 132, 133] and in older adults [134–136]. To prevent falls, modulation of foot placement is a frequently used technique to regulate and restore gait stability [14, 137]. A better understanding of how this modulation of foot placement is controlled is important to optimize fall prevention strategies and reduce fall risk. Particularly relevant are experiments, such as described here, in which one can test how fast a change of foot placement can be achieved (for example to avoid stepping in a pool of water one suddenly observes). Thus, it is essential to have baseline data on young adults before applying the challenging experiments to populations at risk. From the present results it can be concluded that such double-step experiments are likely to be feasible for these latter groups, given appropriate levels of time pressure.

Conclusion

While the principle of minimization of foot displacement is believed to be an important determinant guiding obstacle avoidance strategy selection, step adjustment strategy choices conflicting with this principle have often been attributed to prioritization of safety (e.g. [9, 68]. Our data on the variable ability of young adults to successfully execute certain adjustments indicate that these safety concerns are warranted. Namely, our data clearly show that the ability to execute movement adjustments depends on the direction of the trajectory adjustment. While some obstacle avoidance strategies might be more detrimental for balance than others, any unsuccessful obstacle avoidance is even more dangerous. Therefore, our data indicate that choosing different leg movement adjustments for

obstacle avoidance comes with different risks and strategy choice might not depend exclusively on environmental constrains. In line with the idea of prioritizing safety, the used obstacle avoidance strategy choice might be a trade-off between the environmental factors (i.e., the cost of a specific adjustment) and individuals' ability to execute a specific adjustment with success (i.e., the associated execution risk).

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PART 2: STEP ADJUSTMENTS DURING TRIP RECOVERY

5 FAST ONLINE CORRECTIONS OF TRIPPING RESPONSES

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Abstract

Tripping over obstacles is one of the main causes of falls. One potential hazard to actually fall when tripped is inadequate foot landing. Adequate landing is required to control the body's angular momentum, while avoiding dangerous surfaces (slippery patch, uneven ground). To avoid such dangers, foot trajectory needs to be controlled by inhibiting and adjusting the initiated recovery foot path during a tripping reaction. We investigated whether such adjustments can be made without jeopardizing balance recovery.

Sixteen healthy young adults (25.1±3.2 years) walked at their comfortable speed over a walkway equipped with 14 hidden obstacles. Participants were tripped 10 times in between a random number of normal walking trials; 5 trips included a projection of a forbidden zone (FZ, 30x50 cm) at the subject's preferred landing position. Participants were instructed to land their recovery foot outside the FZ, if the FZ was presented. Responses were evaluated in terms of foot position and body angular momentum at and following recovery foot landing.

Participants successfully landed their recovery foot outside the FZ in 80% of trials, using strategies of either shortening their recovery steps (84%) or side stepping (16%). Their performance improved over trials, and some participants switched strategies. Angular momenta of the adjusted steps remained small at and following recovery foot landing.

Young adults can quickly change foot trajectory after tripping by using different strategies and without detrimental consequences on balance recovery, in terms of the angular momentum. These results open possibilities for training of tripping reactions.

Keywords

Gait perturbation, stability, accidental falls, motor inhibition, obstacle avoidance, angular momentum

Introduction

Movement inhibition is commonly seen in human behavior [27, 98] and is reflected in fast online corrections and movement adjustments in response to external perturbations [18, 138, 139]. Previous work in this field focused mostly on adjustments of arm movements towards a target [13, 138–140] using perturbations such as target shifts [18, 138], and visual and proprioceptive feedback manipulations [13, 141, 142]. However, very little is known about fast corrections during leg movements, such as gait, although these are very important for successful ambulation. Some attempts were made to study online adjustments of leg movements, mostly during obstacle avoidance [5, 67, 94, 101] and step initiation [7]. Yet little is known with respect to alternate foot placement after tripping. This is an important issue however, since the occurrence of a fall can be linked to improper placement of the foot after tripping [82, 143]. In daily life, this proper placement can be difficult in case one has to avoid stepping on "risky" surfaces, like uneven ground or a rainy patch. If fast online adjustments of tripping reactions are possible, this would open possibilities for training and fall prevention in the growing population of older adults [144–146].

Tripping over obstacles has been shown to be one of the dominant causes of falls in older adults [11, 147–149] and mechanisms of tripping have been widely explored [78–81, 85, 88, 90, 143, 150, 151]. In general, following a trip, flexion or extension movements of the tripped foot are observed [85] and switching between these two types of responses has been reported in some individuals [78, 89, 90], suggesting that online adjustments of tripping responses might be possible, probably in order to reduce the risk of falling. An adequate response to a tripping perturbation is needed to reduce the forward angular momentum that the body obtains from impact with the obstacle [88, 152, 153]. Balance can be recovered after tripping by control of trunk movement [88, 143], generating rapid forces in the support leg during push-off [80, 81], and proper placement of the recovery foot [77, 143, 153]. The latter seems especially important as placing the recovery foot anterior to the center of mass (COM) can generate a moment that counteracts the body's forward rotation [77, 88, 143, 153]. Furthermore, this ability is often impaired in older adults, and especially in older fallers, who have been shown to generate less adequate push-off forces when tripped in comparison with healthy young adults. These inadequate push-off forces result in short recovery steps that insufficiently reduce the body's angular momentum, thus increasing the chance of falling [82]. Adjustments of recovery step length might thus be beneficial to avoid falling, but whether or not changes to foot positioning after a trip are possible is not known, as none of the aforementioned studies constrained foot positioning after tripping. If these changes are indeed possible foot positioning after perturbations might be trainable, for

example by teaching subjects how to improve their tripping response or use safe methods for falling if recovery proves impossible [74].

The main aim of our study was to establish whether young adults can adjust their tripping responses and whether this affects balance recovery. In order to do so, we assessed whether people can alter their preferred foot landing position in response to a visual forbidden landing zone (FZ) presented at trip onset. The FZ represents a virtual obstacle that needs to be avoided during trip recovery. Based on previous reports on (incidental) step trajectory adjustments during obstacle avoidance [66, 94] and tripping recovery [78, 89, 90], we hypothesized that our subjects would be able to adjust their recovery foot landing position when a FZ is presented. Our secondary aim was to evaluate the step strategies and consequences of step adjustments for balance recovery in terms of angular momentum.

Methods

Sixteen healthy young adults (age 25.1±3.2 years, height 178.4±8.8 cm, weight 73.2±12.9 kg, 6 females) participated in this study after signing informed consent. Subjects had no walking problems, normal or corrected to normal vision and were able to understand the instructions. The study was in accordance with the guidelines of good clinical practice and approved by the local ethical committee. All subjects gave their informed consent prior to participating in the study.

Experimental setup

Subjects walked at their comfortable speed over a walkway (2.5 m wide and 12 m long), equipped with a force plate and 14 obstacles (15 cm high) hidden over a length of one meter (Figure 5.1). Any of these obstacles could be released from the floor causing the subject to trip. The obstacle to be released was selected online by an algorithm based on the subjects' kinematic parameters during obstacle approach. More specifically, upon landing of the subject's left foot in the area next to the obstacles, the obstacle closest to the midline of the left foot was selected and triggered to be released to cause a trip at mid-swing of the right leg. This impact at mid swing elicited an elevating strategy, meaning that subjects made a recovery step with the foot that hit the obstacle by lifting it over the obstacle [85]. We mixed ten tripping trials with a number (3 - 15) of normal walking trials so that the subjects never knew whether or not they would be tripped in that specific trial. Normal walking trials in between tripping trials ensured that the subjects regained their normal walking pattern [154] and no significant changes in normal gait parameters were observed after the first trip. Participants were encouraged to maintain their preferred velocity as shown at the start of the experiment. To check for possible anticipatory gait changes during the tripping trials, we calculated walking speed for

the stride prior to obstacle contact (see below) and toe clearance as vertical position of the 2nd toe tip at obstacle contact.

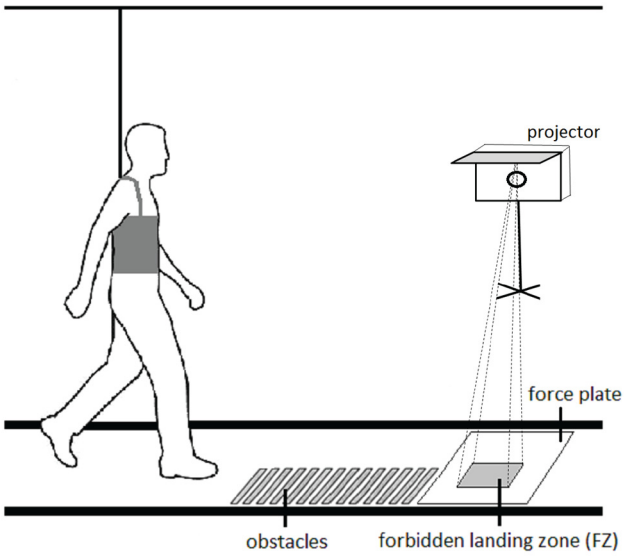

Figure 5.1. Experimental setup. Subjects walked at their comfortable speed on a walkway equipped with a force plate and 14 obstacles. The obstacles were embedded in the flooring and could be released causing the subject to trip at mid swing. In 5 out of 10 tripping trials, a forbidden zone (FZ) was projected at trip onset onto the floor at the subject's preferred recovery step landing position, relative to the selected obstacle. Subjects were instructed to regain their balance following a trip, but avoid landing their foot in the FZ if presented.

Subjects wore a safety harness attached to a ceiling-mounted rail, protecting them from falling in case they were not able to regain balance after a trip. The safety ropes provided enough slack for unrestrained motion, and a spring, in series with the ropes, ensured smooth restraint in case of a fall. The tripping setup was described in more detail by Pijnappels and co-workers [80].

The experiment consisted of two tripping conditions: 'normal tripping' trials and tripping with a presentation of a FZ (T-FZ). The FZ was a 30 cm wide and 50 cm long rectangle projected onto the floor by a generic projector. The FZ size covered the group variability of the recovery foot landing positions of 10 subjects from previous experiments [80–82]. The FZ was triggered 100 ms prior to the trigger for obstacle release and was individually positioned at the participant's average recovery foot landing position during normal tripping.

Following familiarization with the setup and the safety harness, three normal tripping trials were performed, with the subjects instructed to regain balance in any

way that comes naturally. Average recovery foot landing position relative to the obstacle was calculated based on the kinematic data of the foot and used to position the center of the FZ for each participant individually. For the following trials, the subjects were instructed to regain their balance in case of a trip, but to avoid stepping into the FZ if present. Seven more trips (5 T-FZ and 2 'normal' trips) and five trials that included only the FZ without a trip were performed in a pseudorandom manner. The latter condition was used to prevent subjects from associating the FZ with tripping and was not analyzed.

Full body kinematic data were collected at a sample rate of 50 samples/s using an Optotrak system (Northern Digital Inc., Waterloo, Ont., Canada) consisting of a 4x3 camera array. Following anthropometric measurements, 12 clusters of three infrared LED's (Light Emitting Diodes) were attached to the body segments (lower arms, upper arms, lower legs, upper legs, feet, trunk, and pelvis) and a pointer was used to indicate 36 anatomical landmarks. This allowed for reconstruction of the subject's body using a 3D full body kinematic model [155]. Kinetic data were collected using a custom-made strain gauge force plate of 1x1m (sample rate of 200 samples/s), embedded into the walkway in the area where the recovery foot landed.

Data analysis

Ten tripping trials (of four subjects) were excluded from the analysis due to recovery steps using the left foot. Avoiding the FZ was not a challenge in these trials since the FZ was positioned based on the assumption that the right foot would be elevated for the recovery step. The two normal trips mixed with the T-FZ trials served as 'catch' trials and were treated as a separate group in the analysis, as these could have been influenced by the FZ trials. Five T-FZ trials were compared to the first three normal trips (T trials) and the two 'catch' trip trials (TC trials). Kinematic data were filtered using a 2^{nd} order zero lag Butterworth filter with a cutoff frequency of 5 Hz.

Walking speed was calculated from the displacement of the COM in the stride (defined as the time between two heel strikes of the left foot) prior to obstacle contact. Then, we calculated the spatial and temporal parameters of the recovery step. The timing of subject's contact with the obstacle was determined as the local minimum of foot acceleration in the walking direction. The force plate was unloaded prior to the recovery step, so the time of recovery foot landing was identified as the onset of a sudden increase in the vertical force. Manual correction of the recovery foot landing time was needed for one subject, as he performed two steps onto the force plate. Recovery step duration was defined as the time between obstacle contact and recovery step landing. Foot position at landing was determined from the kinematic data as the virtual line connecting the calcaneus and the tip of the second toe. If this line fell fully outside of the FZ, the avoidance was considered successful.

In case of a successful avoidance of the FZ, the step was classified into one of the following strategies: step lengthening, step shortening or side stepping [64] based on the position of the foot at landing (Figure 5.2). The absolute Euclidean distance between the FZ center and center of the line representing the foot was calculated.

Finally, to quantify the effects of adjustments on balance recovery, angular momentum (ANGMOM) of the body around the COM was calculated using a 3D full body kinematic model [155], normalized to bodyweight and quantified at trip onset, landing and 0.3 s after landing. Additionally, to get insight into the amount of rotation during the recovery step and after landing we calculated the areas under the angular momentum curve from obstacle contact until landing (AUC-CL) and from landing until 0.3 s after landing (AUC-AL).

Data processing was performed using MATLAB 2011b (Mathworks, Natick, MA, USA).

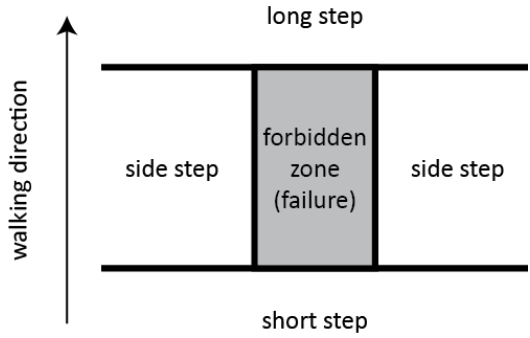

Figure 5.2. Strategies used for FZ avoidance. Trials in which the subjects successfully avoided landing their foot into the FZ were classified based on the position of the foot at landing. If the subject used a large step to step over the FZ with the full foot the trial was termed step lengthening, if a short step was made, such that the subject landed their full foot in front of the FZ, the trial was termed a step shortening, and all other successful trials were defined as side stepping. Unsuccessful trials were the trials in which any part of the foot, defined as a virtual line connecting the calcaneus and the tip of the second toe, overlapped with the FZ.

Statistical analysis

Average step duration, absolute distance between the center of the foot and center of the FZ, toe clearance at obstacle contact, and walking speed were compared between T, TC, and T-FZ conditions using paired samples t-tests.

Generalized estimating equations (GEE) were used for analysis of success rates, strategy choices, and angular momenta. GEE is a robust method of estimating the parameters of a generalized linear model with a possible unknown correlation between outcomes, used for estimating the average response over the population. The potential effect of learning on success of FZ avoidance was analyzed using a GEE

model with trial ordinal number as a predictor and success as a dichotomous response. The same was done for walking speed as a predictor of success. As different strategies in FZ avoidance were observed, GEE models were used to evaluate effects of body height, walking speed, ANGMOM at trip onset, and trial order on strategy choice. Pearson's correlations were calculated between body height and FZ placement. The ANGMOM at trip onset, recovery step landing and 0.3 s after landing and areas under the angular momentum curve from obstacle contact until landing (AUC-CL) and from landing until 0.3 s after landing (AUC-AL) were analyzed using GEE models with five trip strategies (T trials, TC trials, T-FZ step shortening, T-FZ side stepping, and failed T-FZ trials) as a factor and trial ordinal number and walking speed as covariates. This enabled a comparison between the different strategies, while accounting for possible learning effect and differences in walking speed. Step duration was used as an additional covariate for AUC analyses.

All analyses were performed using SPSS Statistics 20 (IBM, Chicago, IL, USA), with a level of statistical significance set to $\alpha = 0.05$.

Results

Mean walking speed in the stride preceding the trip during the T-FZ trials (1.32 ± 0.10 m/s, $p = 0.005$) and TC trials (1.33 ± 0.09 m/s, $p = 0.013$) was slightly but significantly lower than the speed during the T trials (1.40 ± 0.11 m/s). Although toe clearance at obstacle contact slightly increased from 0.04 m during the T trials to 0.07 m during the TC and T-FZ trials (both $p < 0.001$), trips were successfully elicited given the height of the obstacle of 0.15 m.

Overall, subjects were able to adjust their steps and avoid stepping into the FZ. Subjects failed in 14 (20%) and succeeded in 57 (80%) of the T-FZ trials (Figure 5.3). The adjusted steps, irrespective of being successful or not, lasted shorter than the first three normal trips (T trials: 0.48 ± 0.03 s, T-FZ trials: 0.43 ± 0.03 s, $p = 0.002$, Figure 5.4a) and had a larger distance from the center of the foot to the center of the FZ (T trials: 0.10 ± 0.03 m, T-FZ trials: 0.43 ± 0.12 m, $p < 0.001$, Figure 5.4b). Recovery steps in the last two normal 'catch' trips (TC trials) also differed from the first three normal trips (T trials): they were of shorter duration (0.45 ± 0.03 s, $p = 0.003$) and had a larger distance from the center of the foot to the center of the FZ (0.29 ± 0.16 m, $p < 0.001$). However, this distance was significantly smaller than for the T-FZ steps ($p < 0.001$), although the TC and T-FZ steps did not differ in duration.

Performance on the T-FZ trials significantly improved over trials, from 60% of successful FZ avoidances in the first, 73% in the second, 80% in the third, 93% in the fourth and 100% success rate in the final, fifth trial ($p < 0.001$, Figure 5.4c). The GEE model revealed no effect of walking speed on success rate.

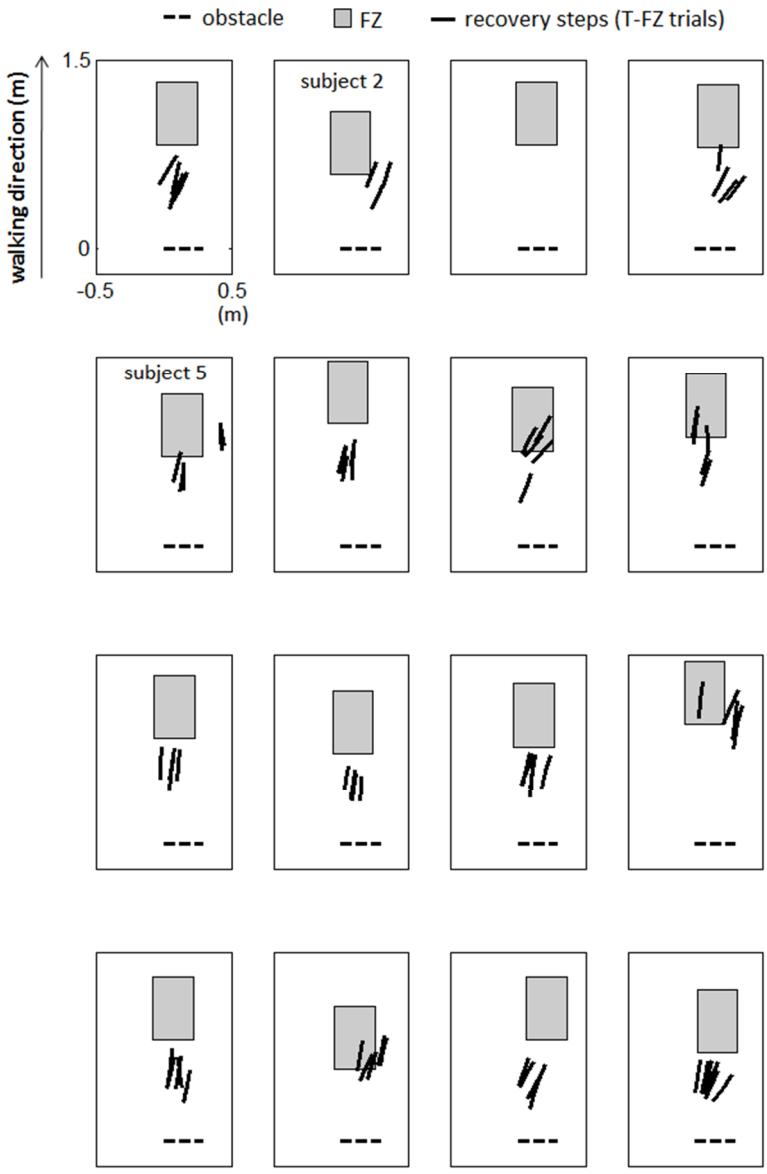

Figure 5.3. Individual responses to the T-FZ trials. All subjects succeeded in avoiding the FZ at least once, although individual differences in success rates are evident. Note that two subjects changed strategies during the experiment (subjects 2 and 5). One of these can be attributed to the strategy definition used (subject 2) whereas the other (subject 5) reflects a change in behavior. Ten tripping trials (of four subjects) were excluded from the analysis, which left subject 3 without any T-FZ trials. Trials were excluded due to subjects using the left foot for recovery steps, which made avoiding the FZ easy, as it was positioned with an expectation of subjects using an elevating strategy and the right foot.

Strategies

Different strategies were used for successful step adjustments. Out of the 57 successful T-FZ trials, step shortening was observed in 48 (84%) trials and side steps (all in lateral direction) were observed in 9 (16%) trials. Long steps (over the FZ) were not observed. Strategy choice was not associated with trial number, walking speed, or ANGMOM at trip onset, but it was significantly associated with subject's body height (GEE $p = 0.035$, $\exp(\beta) = 0.858$), meaning that a side step was 14% less likely to occur with each additional cm in body height. This can be explained by the fact that the FZ was positioned closer to the tripping obstacle for shorter subjects, based on their absolute shorter normal recovery steps during the T trials, as evident from the correlation between the subjects' body height and the FZ position (Pearson $r = 0.623$, $p = 0.010$).

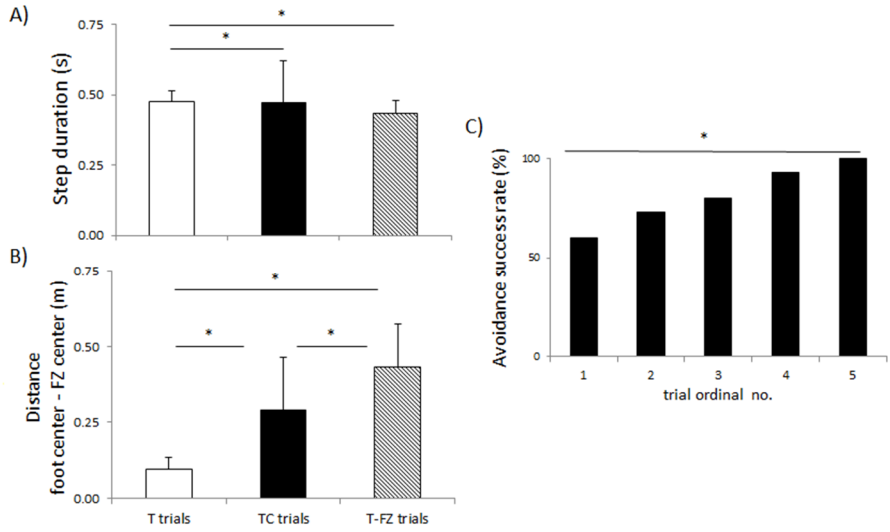

Figure 5.4. Average step duration for T, TC, and T-FZ trials (a), distance from the center of the foot to the center of the FZ (b) for T, TC, and T-FZ trials and percentage of successful T-FZ trials per trial ordinal number. Error bars denote standard deviations and * denotes statistical significance ($p < 0.05$).

Angular momentum

Typical examples of ANGMOM curves in all three planes are shown for a T trial (Figure 5.5a) and T-FZ (step shortening, Figure 5.5b). Rotation in the horizontal plane was minor so the analysis focused on frontal and sagittal planes. Average amounts of ANGMOM, AUC-CL and AUC-AL are shown in Table 5.1. Group angular momentum

data are shown in Figure 5.6 and it can be seen that the magnitude of changes in the angular momentum was small.

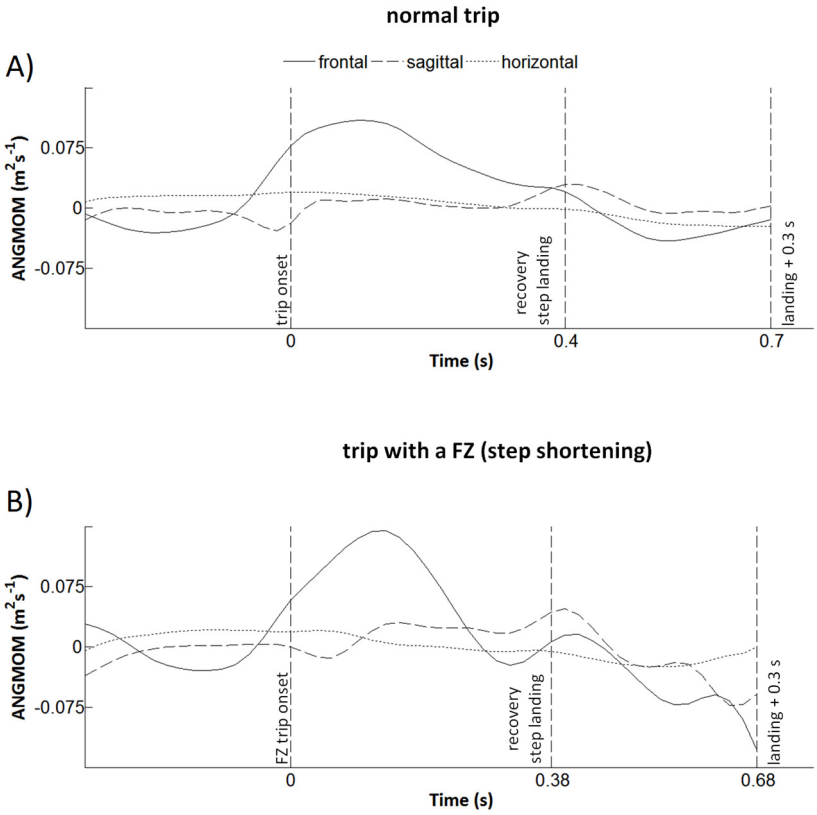

Figure 5.5. Angular momentum around the COM (ANGMOM) normalized to subjects' body weight. Typical ANGMOM curves in the frontal, sagittal and horizontal planes for a 'normal trip' before the first presentation of the FZ (a) and a successful short step avoidance of the FZ (b). Vertical lines denote timings of trip onset, recovery foot landing and 0.3 s after recovery foot landing.

Although most subjects preferred step shortening, this type of strategy did not severely affect the angular momentum compared to normal trips; especially in the sagittal plane, where largest effects were expected for step shortening, only small differences in angular momenta were observed.

According to the GEE model, the average ANGMOM at obstacle contact was associated in the frontal plane with strategy ($p = 0.003$) and in the sagittal plane with covariates walking speed ($p = 0.003$) and trial ordinal number ($p = 0.046$). Average amounts of ANGMOM at landing were associated with walking speed ($p = 0.006$) and

strategy (p = 0.049) in the frontal plane. ANGMOM 0.3 s after landing was associated in the frontal plane with strategy (p = 0.006) and in the sagittal plane with strategy (p = 0.040) and trial ordinal number (p = 0.038). Note that both at and 0.3 s after landing, the average differences in magnitudes of ANGMOM were small for all strategies used.

AUC-CL in the frontal plane was associated with trial ordinal number (p = 0.001), walking speed (p = 0.048), and strategy (p = 0.049). In the sagittal plane AUC-CL was associated with step duration (p < 0.001) and strategy (p = 0.007). In the 0.3 s following recovery step landing AUC-AL and strategy were associated in the frontal plane (p < 0.001) and borderline significantly associated in the sagittal plane (p = 0.054).

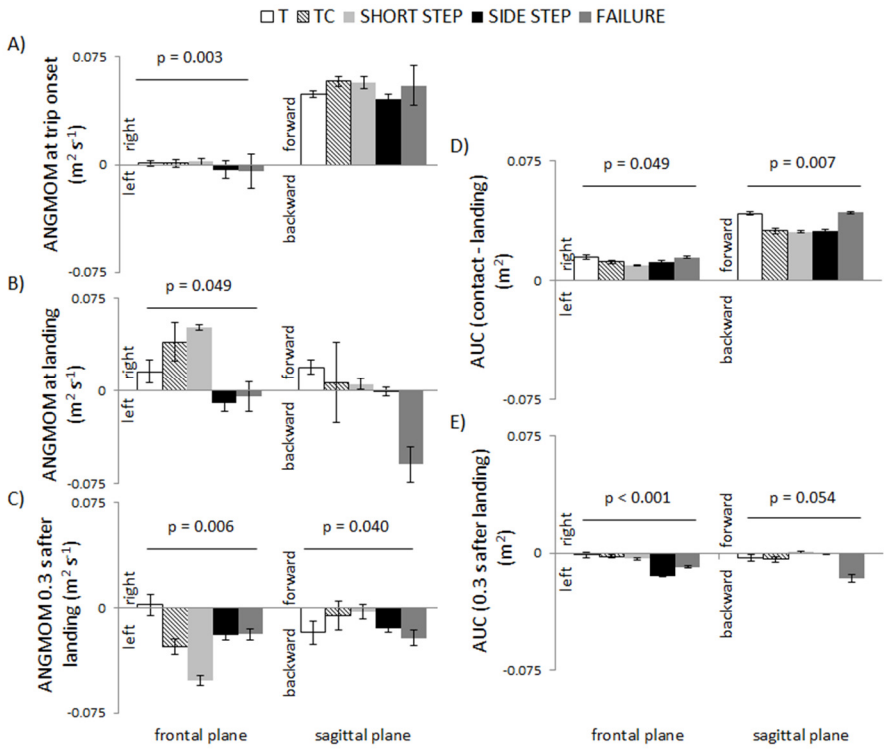

Figure 5.6. Angular momentum around the COM (ANGMOM) normalized to subjects' body weight. Group average amounts of ANGMOM at trip onset (a), landing (b) and 0.3 s after landing (c), and areas under the ANGMOM curve (AUC) from obstacle contact until landing (d) and from landing until 0.3 s after landing (e). Error bars denote standard errors of the mean and statistically significant effects of strategy are denoted by their p values (GEE p < 0.05). Note that the effect of strategy on the sagittal plane AUC 0.3 s after landing is only borderline significant.

Table 5.1. Average amounts of angular momentum (ANGMOM) at trip onset, recovery step landing and 0.3 s after recovery step landing and areas under the angular momentum curve from contact to recovery step landing (AUC-CL) and for 0.3 s after recovery step landing (AUC-AL) in the sagittal and frontal planes. Data are shown for 'normal' tripping trials before the first presentation of the FZ (T trials), 'normal' tripping trials after the first presentation of the FZ (TC trials), successful forbidden zone (FZ) avoidances using a step shortening or side stepping, and unsuccessful FZ avoidances (failed T-FZ trials). Amounts are shown in $m^2 s^{-1}$ (ANGMOM) and m^2 (AUC) as mean ± SD.

		T trials	TC trials	Step shortening	Side stepping	Failed T-FZ trials
at trip onset						
ANGMOM	frontal	0.001 ± 0.014	0.001 ± 0.014	0.002 ± 0.014	-0.004 ± 0.011	-0.005 ± 0.014
	sagittal	0.049 ± 0.016	0.058 ± 0.018	0.057 ± 0.018	0.046 ± 0.018	0.055 ± 0.023
at recovery step landing						
ANGMOM	frontal	0.016 ± 0.119	0.040 ± 0.087	0.052 ± 0.028	-0.010 ± 0.078	-0.005 ± 0.145
	sagittal	0.019 ± 0.072	0.007 ± 0.181	0.006 ± 0.052	-0.001 ± 0.042	-0.059 ± 0.171
AUC-CL	frontal	0.015 ± 0.014	0.012±0.005	0.010 ± 0.006	0.012 ± 0.009	0.015 ± 0.010
	sagittal	0.042 ± 0.013	0.031±0.011	0.031 ± 0.012	0.031 ± 0.014	0.043 ± 0.009
0.3 s after recovery step landing						
ANGMOM	frontal	0.002 ± 0.092	-0.028 ± 0.032	-0.052 ± 0.040	-0.019 ± 0.045	-0.019 ± 0.047
	sagittal	-0.018 ± 0.101	-0.006 ± 0.057	-0.003 ± 0.063	-0.015 ± 0.030	-0.022 ± 0.069
AUC-AL	frontal	-0.001 ± 0.022	-0.002±0.005	-0.004 ± 0.007	-0.015 ± 0.008	-0.009 ± 0.010
	sagittal	-0.003 ± 0.026	-0.004±0.011	0.001 ± 0.010	-0.001 ± 0.006	-0.016 ± 0.029

Discussion

We investigated whether and how young adults can adjust their tripping responses and secondly, we explored the consequences of adjustments on balance recovery in terms of angular momentum. As hypothesized, subjects were able to adjust their tripping responses and avoid landing in the FZ. Although individual differences in success rates were present, all subjects succeeded at least once. In their attempts, either successful or unsuccessful with respect to avoiding the FZ, none of our subjects lost balance, and only small changes in the magnitudes of angular momenta were observed.

Adjustment strategies and their consequences

We have shown the ability of young adults to execute online adjustments of their trip recovery step trajectories in response to a visual cue (FZ) in the environment. These findings are in line with previous work on obstacle avoidance, showing the ability to execute two stage corrections of foot placement when a second obstacle is presented in the landing area of the initial obstacle crossing step [94]. Furthermore,

our results confirm incidental reports of individuals changing response step trajectories based on environmental constraints during obstacle avoidance [66] and tripping recovery [78, 89, 90].

Our FZ can be considered a virtual obstacle appearing in one's path following a trip. The FZ approach is similar to that taken in the obstacle avoidance literature by Moraes and co-workers [66, 68] and by Chen and co-workers [64, 65], who investigated avoiding a virtual FZ during normal walking. They showed that FZ avoidance can be achieved by either step lengthening to step over the FZ, step shortening to step in front of the FZ, or by stepping to the side [64]. In our case, to avoid landing into the FZ, one needs to utilize one of these obstacle avoidance strategies, while recovering from a trip. We observed that step shortening was the dominant strategy for FZ avoidance, used in 84.2% of all successful FZ avoidance trials. This finding is surprising at first sight, as we expected step shortening to be less beneficial in terms of time and angular momentum.

Firstly, as established in obstacle avoidance experiments, step lengthening would allow for more time to implement a step adjustment than shortening. In obstacle avoidance, this time is termed available response time (ART) and defined as the time between obstacle appearance and the time of the foot's collision with the obstacle if there is no avoidance reaction. In our experiment the FZ is a virtual obstacle and the tripping recovery step is in fact an obstacle avoidance step. Hence, because the virtual obstacle (FZ) is presented at trip onset and collision with the FZ would occur at recovery step landing if no adjustment is made, the duration of a 'normal tripping' recovery step (i.e., T trials) is equivalent to ART. Research on obstacle avoidance in young adults [9, 64] reported a switch from using predominantly step shortening to lengthening when time available to respond (ART) increases above 250-300 ms. In our case, timing does not seem to be a likely explanation for the occurrence of step shortening: the average durations of both the T steps and T-FZ steps were in the range where young adults prefer step lengthening during obstacle avoidance (T trials 476 ms, T-FZ trials 434 ms).

Secondly, in terms of angular momentum, long recovery steps are beneficial for reducing the amount of angular momentum generated by the trip in the sagittal plane [77, 82, 88, 90, 143], and step shortening could be potentially destabilizing as it could result in increased angular momentum at landing [9, 82, 143]. In our experiment, only minor effects of step shortening were seen on angular momentum compared to normal tripping and our subjects were able to regain balance, as indicated by the small magnitudes of angular momenta in both sagittal and frontal planes at and following recovery step landing.

The main reason why our subjects preferred step shortening was likely the size of the FZ (30 cm wide and 50 cm long). We selected a FZ large enough to cover the

group variability in the landing foot positions obtained from previous tripping experiments [80–82], to ensure that successful T-FZ trials were the result of recovery step adjustments and not chance. Probably, the FZ was positioned at such a distance and was so long, that it was physically too challenging for subjects to avoid it by further lengthening their steps. Namely, on average, the far edge of the FZ was located at 1.28 m from the obstacle. In comparison, the average step length preceding the trip was 0.75 m. This means that a successful crossing of the FZ with a long step would require a lengthening of the step by about 0.52 m (i.e., 70%).

Our subjects used two strategies for successful FZ avoidance (step shortening and side stepping). Strategy selection was related to body height; taller subjects mostly used step shortening, while shorter subjects more often used side steps. This effect of body height on strategy choice may have been caused by the relative distance between the obstacle and the FZ. Shorter subjects made shorter recovery steps during the T trials and therefore their FZ was positioned closer to the tripping obstacle. Hence, these subjects probably preferred side stepping because the limited space between the obstacle and FZ would make step shortening too challenging for them. However, based on the magnitudes of angular momenta of the adjusted steps, we believe that recovery step adjustments (irrespective of the strategy used) did not threaten balance recovery following a trip. Our reasoning is based on the fact that, although strategy was significantly associated with angular momentum, the magnitudes of the measured angular momenta were small compared to previously reported data of successful trip recoveries in young adults. In our experiment the largest changes in angular momentum between trials with and without a FZ were seen at landing for step shortening in the frontal plane and for failed T-FZ trials in the sagittal plane. However, the angular momenta of these adjusted steps were still smaller than previously reported values for successful trip recovery in young adults using the same setup [82, 156], both in the sagittal plane (>0.1 m^2s^{-1}; in our experiment -0.06 m^2s^{-1}) and in the frontal plane (-2.99 m^2s^{-1}; in our experiment 0.05 m^2s^{-1}). Therefore we believe that these magnitudes of angular momenta do not present a problem for healthy young subjects to successfully recover from the trip, as was the case in our experiment where none of the subjects fell.

Learning effect and its implications

Although each subject was able to adjust recovery steps, not all of our subjects were successful in avoiding the FZ in all of the trials. However, they all improved performance with practice, and were able to avoid the FZ in at least one trial. Success rates significantly improved over trials, from 60% of successful FZ avoidances in the first, to a 100% success rate in the final, fifth T-FZ trial.

Learning effects were also reflected in the two normal ‘catch’ trips in between the T-FZ trials. These trips differed from the first three normal trips in walking speed, toe

clearance at obstacle contact, and recovery step duration. Most importantly, the average distance from the center of the foot to the center of the FZ increased by 0.19 m from the first three normal trips. Landing at a more remote position from the center of the FZ is the appropriate strategy to assist avoiding a FZ in case it would appear and indeed, if the FZ had been presented in these trials, our subjects would have avoided it successfully using step shortening in 11 (out of 31) trials. This suggests that anticipation affected the tripping response even if there was no FZ and illustrates that learning occurred, in line with previous work using similar tripping responses [157].

Our data are in line with several studies that reported anticipation and learning effects following trips and slips. For example, following a contact of the trailing limb with an obstacle, subjects increased their trail limb toe clearance and peak toe elevation [151]. In another study [87], after being exposed to eight consecutive overground trips, young adults exhibited changes in their kinematic parameters both in anticipation of the trip (reduced COM velocity and forward instability and increased toe clearance) and during trip recovery (decreased maximal trunk flexion, increased hip height, posterior shift in the COM position and decreased COM velocity). These adjustments were beneficial for reducing angular momentum and regaining balance, but were based on trip anticipation and not on applying a new strategy or responding to environmental constraints. The same group [158] reported improvements in 'fall-resisting skills' when young adults were exposed to blocks of consecutive trips and slips. However, a major limitation of these experiments was a decrease in walking speed observed prior to the trip of interest, which was not controlled for in the data analysis. This limits the conclusions that could be drawn, as walking speed at impact largely influences success of tripping recovery [143, 152]. Several other groups have reported improvements in tripping responses following a number of actual [82] or simulated trips [144]. Overall, these findings seem to indicate a possibility for learning to improve tripping responses. While a strong limitation here is that in everyday life it is impossible to continuously anticipate a possible trip or slip, this should not discourage future training of older adults.

Older subjects have frequently been shown to make recovery steps that are too short for successful balance recovery [82]. Therefore, if older adults are also able to adjust and improve their tripping responses such that they lengthen their recovery steps, this might potentially reduce the number of falls. The feasibility of such an approach is supported by the changes in the kinematics of tripping responses of healthy older adults following a training consisting of simulated slips on a treadmill [144] and by the ability of older adults to increase their step length following five anticipated trips simulated by treadmill accelerations from quiet standing [159]. Training consisting of such treadmill accelerations was shown to decrease the number of falls [145, 146]. However, in our experiment young adults did not use step lengthening to avoid

landing in the FZ, probably due to its size and position. Whether or not older adults would be able to adjust their tripping responses in order to avoid landing in the FZ, and whether they would be able to lengthen their recovery steps to do so, needs further investigation.

Conclusion

Our study showed that young adults are able to execute fast online adjustments of trip recovery steps in order to avoid landing on a FZ and that they do so by using different strategies. The adjustments (irrespective of strategies) do not seem to threaten balance recovery, in terms of the angular momentum at, and following, recovery foot landing. Subjects improved their success rates over trials, could switch between strategies, and adjusted their responses even when no FZ was presented. These behavioral results serve as a basis for further research on the underlying mechanisms for inhibition and adjustments during tripping and on the feasibility to include trip recovery training for fall prevention in older adults.

Acknowledgements

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6 TWO STAGE MUSCLE ACTIVITY RESPONSES IN DECISIONS ABOUT LEG MOVEMENT ADJUSTMENTS DURING TRIP RECOVERY

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Abstract

Studies on neural decision making mostly investigated fast corrective adjustments of arm movements. However, fast leg movement corrections deserve attention as well, since they are often required to avoid falling after balance perturbations. The present study on tripping responses aimed at elucidating the mechanisms behind fast corrections of tripping responses by analyzing the concomitant leg muscle activity changes. This was investigated in seven young adults who were tripped and took a recovery step by elevating the tripped leg over the obstacle. In some trials, a forbidden landing zone (FZ) was presented behind the obstacle, at the subjects' preferred foot landing position, forcing a step correction to avoid landing in the FZ. Muscle activity of the tripped leg gastrocnemius medialis (iGM), tibialis anterior (iTA), rectus femoris (iRF), and biceps femoris (iBF) muscles was compared between normal trips, trips with a FZ, and 'catch' trials (normal trips presented in between trips with a FZ). When faced with a real or expected (catch trials) FZ, subjects shortened their recovery steps. The underlying changes in muscle activity consisted of two stages. The first stage involved reduced iGM activity, occurring at a latency shorter than voluntary reaction, followed by reduced iTA and increased iBF and iGM activities occurring at longer latencies. The fast response was not related to step shortening, but longer latency responses clearly were functional. We suggest that the initial response possibly acts as a "pause", allowing the nervous system to integrate the necessary information and prepare the subsequent, functional movement adjustment.

Keywords

Stumbling, balance perturbations, obstacle avoidance, muscle activity, online corrections

Introduction

In the study of neural decision making, one of the prevailing issues is how the brain manages the task of making very fast corrective movements. In this domain, mainly arm movements towards a target have been studied [13, 138–140]. Typically a perturbation was introduced, such as a target shift, requiring the subject to make a correction during an ongoing movement [18, 138]. These corrective responses are very fast and occur below the latency for initiation of voluntary movements [119–121]. To explain these fast reactions, some authors proposed a fast pathway over the parietal cortex [122, 160], while others suggested a subcortical pathway [19].

Online correction of leg movements has received less attention, possibly because such experiments are more difficult due to gravity and postural challenges. Only few studies have addressed the issue of leg movement corrections by investigating step initiation from quiet stance, when subjects had to step on a target that shifts, similar to the dual step experiments for the arm [7, 50, 51]. In line with the findings from arm movement research, these experiments indicated that movement corrections during step initiation could occur at very short latencies, thereby suggesting that subcortical mechanisms could be involved [50]. During gait, making corrections to foot trajectory and landing position is even more relevant and an ecologically important issue, since one often needs to quickly correct an ongoing step in order to avoid dangerous foot landing areas (e.g., a hole in the pavement) to prevent falls. A number of studies addressed avoidance of suddenly appearing obstacles during gait [5, 9, 58, 63, 64, 66, 94, 101] and, similar to step initiation, leg movement corrections occurring at short latencies were found, supporting the idea of a subcortical pathway [58]. Behaviorally, step corrections in order to avoid obstacles are accomplished in several ways. Most often step lengthening (i.e., stepping over the obstacle) or step shortening (i.e., stepping in front of the obstacle) were reported [9, 64]. One could imagine that the avoidance reactions would be “ballistic” in the sense that they would be immutable once triggered. However, this is not the case, since obstacle avoidance strategies can be altered online. In particular, young adults could correct their step trajectory during the process of obstacle avoidance if a cue was presented to change the landing position [66, 94]. This implies that people have the ability to correct these fast leg movements online.

When people are not able to detect the presence of an obstacle or fail in obstacle avoidance, a trip occurs as their swing leg is obstructed by the obstacle. This results in fast reactions to clear the obstacle and regain balance [77–81, 85, 88, 90, 91, 161]. Humans use two types of recovery strategies: they either lower the obstructed foot immediately and step over the obstacle with the other leg (‘lowering’ strategy), or they elevate the obstructed foot over and place it behind the obstacle (‘elevating’ strategy) [78, 85]. These behavioral responses are driven by muscle activities showing several activity peaks at various latencies. The origin of the earliest muscle

activity related to tripping is unclear, but possible sources are stretch reflexes [161] or startle related activation [162]. In contrast, the activity occurring at a longer latency is easier to understand in terms of decision making, i.e. the longer latency (>110 ms) muscle activity was related to the behavioral outcome. It determined whether the ongoing, perturbed step would be shortened for executing a lowering strategy or lengthened to use the elevating strategy for trip recovery [78, 81].

These behavioral responses had the appearance of triggered responses and raise the question whether such responses are still modifiable, e.g. when facing additional environmental constraints. If tripping responses were completely defined from the onset of collision onward, then one would expect to see a fixed response pattern, not allowing additional changes. A hint that this was not the case and that modifications are indeed still possible was provided by incidental observations of foot trajectory modification during tripping recovery [78, 89, 90] and confirmed in our recent study investigating the ability to correct leg trajectory during trip recovery [131]. In the latter study, subjects were tripped in the swing phase, which induced an elevating balance recovery response. At trip onset, a forbidden landing zone (FZ), was projected at their preferred landing position and, in order to avoid landing their foot on the FZ, subjects had to correct the trajectory of their balance recovery step. The results showed that all young adults tested were able to modify their responses and successfully land their foot outside the FZ. For this they used strategies of either shortening their recovery steps (84 %) or stepping to the side of the FZ (16 %) [131].

These behavioral observations did not answer the question as to how the decision for leg movement correction was made. To address this question, in the present study we analyzed activity of leg muscles involved in the correction. For this study, a subset of successful FZ avoidances was selected, during which the most common leg trajectory correction was made (step shortening). By analyzing muscle activity we aimed to address three specific questions. Firstly, we wanted to describe changes in muscle activity driving the observed leg trajectory adjustments. In order to shorten the normal trip recovery step, we expected additional activation of hip extensors and ankle plantar flexors, leading to an earlier recovery step landing. Secondly, we wanted to evaluate whether these muscle activity changes consist of functionally different components with respect to the observed step shortening. Namely, in analogy with the simple tripping data [78], we expected early responses seemingly unrelated to the behavioral outcome, along with later responses that are in line with the behavioral changes. If this is indeed the case, it might help to better understand the nature of fast decision making processes when adjusting leg trajectory to avoid inappropriate foot placement under time pressure. Finally, we wanted to address the influence of anticipation on the process of decision making for fast leg movement adjustments by analyzing muscle activity changes on ‘catch’ trials, when no movement adjustment was required. Based on our previous analysis of behavioral

data [131] we expected anticipation to influence the adjustment behavior and we wanted to investigate if the underlying mechanisms were similar to those used when adjustments were required.

Methods

Sixteen young adults (age 25.1±3.2 years, height 178.4±8.8 cm, weight 73.2±12.9 kg, 6 females) who had no walking problems, normal or corrected to normal vision and were able to understand the instructions participated in this study. Electromyographic (EMG) data of seven participants (age 24.6±3.2 years, height 180.4±4.9 cm, weight 71.1±10.5 kg, 1 females), who successfully used the step shortening strategy in all tripping trials are presented here and the behavioral data of all subjects are reported in [131]. The study was approved by the local ethics committee (#2013-7) and all subjects gave their informed consent prior to participating.

Experimental setup

A detailed description of the methods has been provided in a previous publication [131], therefore only the main features are repeated here, along with the information concerning the EMG analysis. Subjects walked at comfortable self-selected speed over a walkway (2.5 m wide and 12 m long), equipped with a force plate and 14 obstacles (15 cm high) hidden over a length of one meter (Figure 6.1). Based on the subjects' kinematic parameters during obstacle approach any of these obstacles could be released from the floor causing the subject to be tripped [154]. The trips always occurred at mid-swing of the right leg and elicited an elevating strategy, meaning that subjects made a recovery step by lifting the obstructed (right) foot over the obstacle [85].

Subjects were presented with ten tripping trials in between a random number (3 - 15) of normal walking trials to ensure that they regained their normal walking pattern [131, 154] and to prevent them from knowing whether or not they would be tripped in that specific trial. The experimenter encouraged the participants to maintain the walking velocity that was self-selected at the start of the experiment. Subjects wore a safety harness attached to a ceiling-mounted rail, protecting them from falling in case they were not able to regain balance after a trip. The safety ropes provided enough slack for unrestrained motion, and a spring, in series with the ropes, ensured smooth restraint in case of a fall [80]. None of the participants fell.

The experiment consisted of two tripping conditions: 'normal tripping' trials and tripping with a presentation of a FZ. The FZ was a 30 cm wide and 50 cm long rectangle projected onto the floor by a generic projector and its size covered the group variability of the recovery foot landing positions of 10 subjects from previous

experiments [80]. Due to technical limitations the FZ appeared about 50 – 100 ms prior to obstacle release and was individually positioned at the participant's average recovery foot landing position during normal tripping. Participants were instructed to land their recovery foot outside the FZ, if it was presented.

At the start of the experiment, following familiarization with the setup, three normal tripping trials (T trials) were performed, with the subjects instructed to regain balance in any way that came naturally. Kinematic data of the foot were used to calculate the average recovery step landing position relative to the obstacle and the FZ was centered at the average position of the foot cluster marker at landing for each participant individually. For the following trials, the subjects were instructed to regain balance in case of a trip, but to avoid stepping in the FZ if presented. Seven more trips and five trials that included only the FZ without a trip (FZ trials) were performed in a pseudorandom manner, with normal walking trials in between. Five trips included the FZ (T-FZ trials) and two did not, serving as 'catch' trials (TC trials).

Full body kinematic data were collected at a sample rate of 50 samples/s using an Optotrak system (Northern Digital Inc., Waterloo, Ont., Canada) consisting of a 4x3 camera array. Following anthropometric measurements, 12 clusters of three infrared LED's (Light Emitting Diodes) were attached to the body segments (lower arms, upper arms, lower legs, upper legs, feet, trunk, and pelvis) and a pointer was used to indicate 36 anatomical landmarks. This allowed for offline reconstruction of the subject's body using a 3D full body kinematic model [155]. Kinetic data were collected using a custom-made strain gauge force plate of 1x1m (sample rate of 200 samples/s), embedded into the walkway in the area where the recovery foot landed. EMG data of the ipsilateral (obstructed) leg muscles rectus femoris (iRF), tibialis anterior (iTA), gastrocnemius medialis (iGM) and biceps femoris (iBF) were recorded at a sample rate of 1000 samples/s using a Porti 17 system (TMSi, Enschede, The Netherlands; 22 bits AD conversion after 20 times amplification, input impedance > $10^{12}\Omega$, CMRR > 90 dB for the relevant range of frequencies). The skin was prepared and bipolar surface electrodes were placed in line with the SENIAM guidelines [163].

Data analysis

We selected data from seven subjects who successfully avoided the FZ by step shortening in all T-FZ trials. Analysis of kinetic and kinematic data are described in detail in [131], but briefly: following the offline reconstruction of body segments, the foot was defined as the virtual line connecting the calcaneus and the tip of the second toe. If this line fell fully outside of the FZ at landing, the avoidance was considered successful. The step was classified as step shortening if the foot landed between the obstacle and the FZ [64]. Obstacle contact time was determined as the local minimum of foot acceleration in the walking direction and the time of recovery foot landing was identified as the onset of a sudden increase in the vertical force,

since the force plate was unloaded prior to the recovery step landing. Toe velocity was calculated by differentiation of toe position.

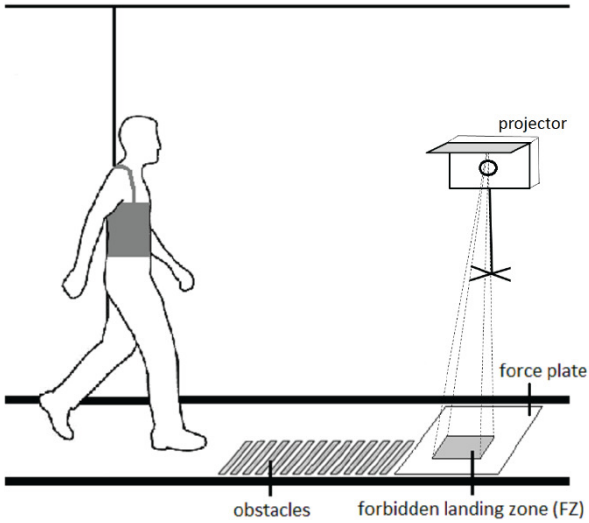

Figure 6.1. Experimental setup. Subjects walked on a walkway equipped with a force plate and 14 hidden obstacles. The obstacles could be released and trip the subject at right mid-swing, causing an elevating recovery strategy. In five out of a total of 10 tripping trials, a forbidden landing zone (FZ) was projected onto the floor at the subject's preferred recovery step landing position, relative to the obstacle causing the trip. Subjects were instructed to regain their balance following a trip, but avoid landing their foot in the FZ, if presented. With permission, reprinted from [131].

EMG data were whitened (fifth order) [164] to reduce the influence of tissue filtering and movement artefacts, Hilbert transformed, and low- pass filtered (third order Savitzky-Golay filter, frame size of 61). EMG data were then aligned to heel strike of the left leg, which served as obstacle and FZ trigger. Average normal walking EMG activity was calculated for each subject (based on five normal walking trials) and subtracted from EMG activity of the T, T-FZ, TC, and FZ trials. The residual FZ trials EMG was not included in the analysis, but served to verify that the participants' EMG signals did not change in response to the visual stimuli alone. This was crucial because the FZ appeared slightly earlier than obstacle contact in T-FZ trials. Finally, the T, T-FZ, and TC trials were aligned to obstacle contact and normalized to maximal EMG activity during normal walking.

Statistical differences between different types of trip trials were analyzed using wavelet-based functional ANOVA (wfANOVA) with trip type (T, T-FZ, and TC) and subject as factors. This method allows to show differences in the shape and magnitude of EMG signals with a high temporal resolution and statistical power by

transforming the EMG signals and running the statistical analysis in the wavelet domain [165]. Following the analysis, significant contrasts were transformed back to the time domain. Level of statistical difference was set to $\alpha = 0.05$. For interpretation, onsets of muscle activity were detected by visual inspection. Responses starting at a latency below 150 ms were considered early, involuntary reactions, while those starting at longer latencies were considered voluntary (Figure 6.2).

All analyses were performed using MATLAB 2011b and 2014b (Mathworks, Natick, MA, USA).

Results

On average, the recovery steps lasted 0.48±0.03 s during the T trials and were shortened to 0.41±0.03 s during the T-FZ trials. Subjects landed the center of their foot 0.09±0.04 m from the position where the FZ would be centered during the T trials and 0.51±0.06 m from the center of the FZ during the T-FZ trials. Surprisingly, the TC trials, which served as 'catch' trials and during which no FZ was shown, also resulted in altered duration of the recovery step (0.43±0.04 s) and positioning of the foot (0.39±0.12 m). In nine out of fourteen TC trials the FZ would have been avoided successfully, if it had been presented. This indicates that anticipation of a forbidden zone influenced the subjects' performance. Therefore special attention was given to the first trial responses, to ensure these are not fundamentally different from the rest (see below).

First trial responses

Overall, subjects' EMG responses were consistent across trials, as can be seen in Figure 6.2 for iGM of a typical subject. However, while fundamentally consistent, with increasing experience (i.e., on later trials) responses started slightly earlier and often decreased in magnitude. This can be seen in Figure 6.2 by comparing the first trial response (black line) to ensuing responses (gray lines), for T and T-FZ trials. A similar pattern was present in the kinematic data of the T-FZ trials, where one can see that the response to the first trial (black line) was fundamentally consistent with responses to ensuing trials (grey lines), although slightly delayed. Additionally, responses to T-FZ trips started earlier than responses to T trials. TC trials, during which no FZ was presented, were also different from T trials and exhibited earlier response onsets, similar to T-FZ trials. However, unlike the T-FZ trials, they showed less activation around the time of landing. Figure 6.2 also illustrates the average normal walking activity on trials without any perturbation and responses during the FZ trials, when no trip occurred, but the FZ was presented. These latter graphs show that there is almost no muscle activity associated with the presentation of the FZ during the time window of interest, i.e., between the average trip onset and recovery step landing of tripping trials. In the data of the typical subject, shown in Figure 6.2,

it can be seen that the iGM responses to the presentation of the first FZ after tripping did not basically differ from the responses seen in later T-FZ trials. This was further confirmed for the other muscles recorded as well.

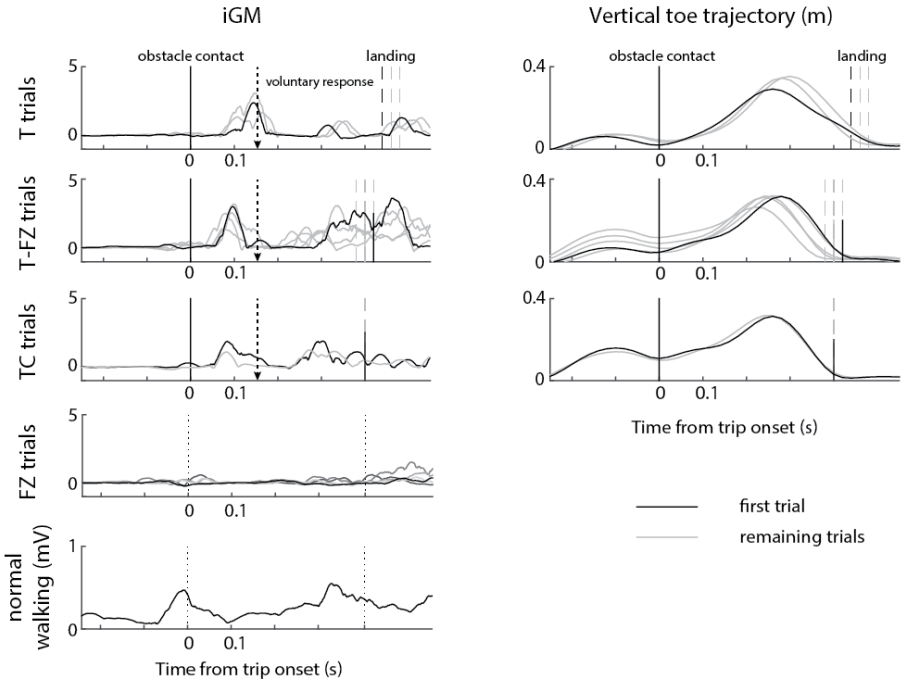

Figure 6.2. Individual iGM activity and vertical toe trajectory of responses to T, T-FZ, and TC trials by a representative subject (subject no. 12). Also shown are iGM muscle activity during FZ trials and average normal walking of the same subject. Data of the first trial are shown in black and of subsequent trials in gray. Black vertical line (at time = 0) indicates obstacle contact and dashed lines indicate recovery step landing, color coded to match the trial order. Note that for some T-FZ and TC trials there is an overlap in the landing time, indicated by a vertical line that is half solid (in the color of the first trial landing at this time) and half dashed (in the color of the second trial landing at this time). Vertical arrows presented in the T, T-FZ, and TC plots indicate latencies of 150 ms. Responses occurring earlier than this are considered early, involuntary responses, while those occurring at longer latencies are considered voluntary. During the FZ trials and average normal walking no trip occurred and the dotted vertical lines indicate expected obstacle contact and recovery step landing, based on this subject's average performance during tripping trials. EMG data of T, T-FZ, TC, and FZ trials are normalized to average normal walking and thus unitless (a value of one indicates that the amplitude of the response was equal to the maximal EMG activity during normal walking in that muscle).

Figure 6.3 illustrates the first trial responses and average of remaining responses of all ipsilateral leg muscles in the same typical subject, for T, T-FZ, and TC trials. Comparing the first trial responses to the average responses, it can be seen that the

response patterns were similar over trials. However, some muscles appeared to be slightly more active in response to the first T-FZ trial compared to average T-FZ, evident by a prolonged activation of iBF and higher amplitudes of iRF. Furthermore, this figure shows that the TC trials shared characteristics of both T and T-FZ trials. Similarly to the first T-FZ trial, the first TC trial showed an early response of iGM coinciding with a reduction in iTA activity, and increased iBF activity prior to the recovery step landing. On the other hand, the pattern of iRF activity resembled that of T trials. Similar changes can be seen in the average responses: both T-FZ and TC trials showed an early reduction in the iTA followed by earlier activations of iGM and iTA, compared to the T trials.

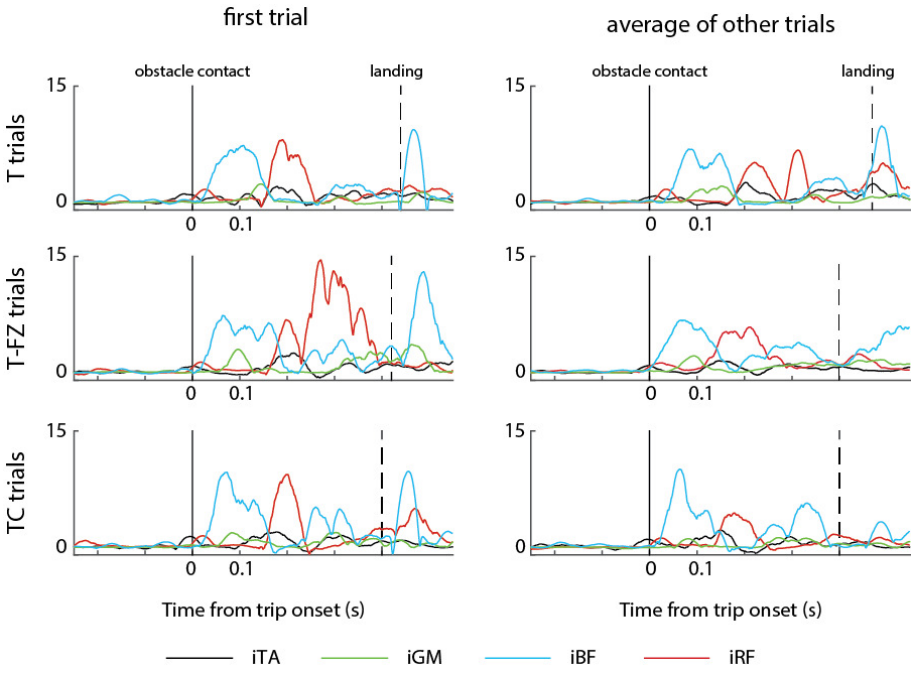

Figure 6.3. Responses of ipsilateral muscles to T, T-FZ, and TC trials by a representative subject (subject no. 12), for the first trial of the type (left) and average of remaining trials (right). EMG data are aligned to obstacle contact, which is indicated by a black vertical line at time = 0. The dashed black vertical line indicates recovery step landing. EMG data are normalized to average normal walking and thus unitless.

Average group responses

Figure 6.4 illustrates group averaged responses to T, T-FZ, TC, and FZ trials. From the kinematic data it can be seen that subjects exhibited consistent step shortening behavior, which is described in more detail below. In response to tripping all muscles

showed activity very close to trip onset and responses were strongest in iRF and iBF. During T trials, amplitude peaks occurred first in iBF (82 ms), followed by iGM (150 ms), iRF (193 ms), and iTA (~205 ms). This order was slightly different during T-FZ and TC trials: activity started with iBF (80 and 72 ms, respectively), followed by iTA (160 and 148 ms, respectively), iRF (193 and 186 ms, respectively), and iGM (350 and 378 ms, respectively). These responses were consistent across subjects, although there was some variability in the magnitude of the response, especially for iRF. Finally, looking at the FZ trials, in most muscles, on average there was no activity associated with the presentation of the FZ in the time between average trip onset and recovery step landing, meaning that the activity seen during the T-FZ trials cannot be attributed to the visual stimulus alone. The only exception was some extra iGM activity seen just prior to expected foot landing. This is probably related to changes in normal walking in response to the FZ, although the FZ was positioned in the expected foot landing area for tripping, which was further away than for normal gait.

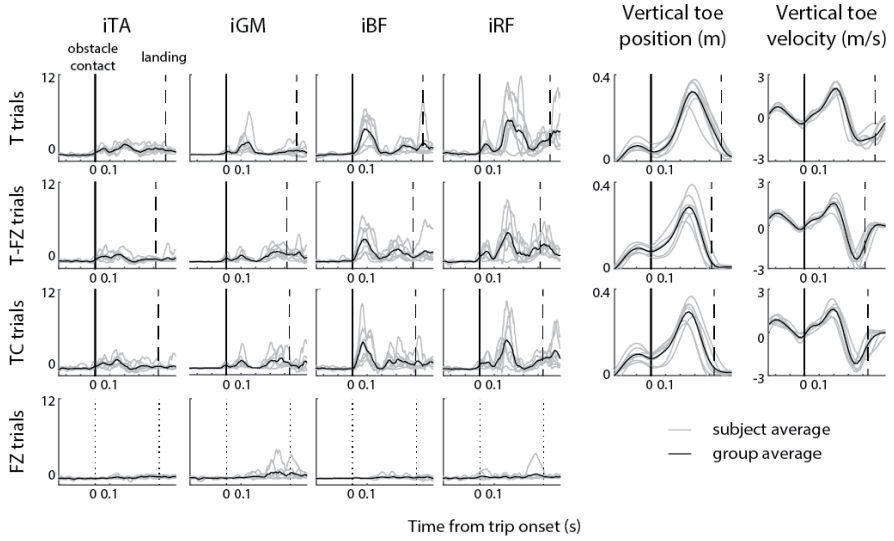

Figure 6.4. Responses to T, T-FZ, TC, and FZ trials for the ipsilateral leg. Subjects' average data are shown in grey and group averages are shown in black. T, T-FZ, and TC signals are aligned to obstacle contact, indicated by a black vertical line at time = 0. Dashed lines indicate average recovery step landing. During the FZ trials no trip occurred and the dotted vertical indicate expected obstacle contact and recovery step landing, based on this group average performance during tripping trials. EMG data are normalized to average normal walking and thus unitless.

Statistical comparisons of kinematics and muscle activity

Statistically significant differences in kinematics and muscle activations in response to T, T-FZ and TC trials are shown in Figure 6.5 (comparison between T and T-FZ trials) and Figure 6.6 (comparison between T and TC trials).

The main kinematic difference between T and T-FZ trials was step shortening in the T-FZ trials (to avoid the FZ). As a consequence the T-FZ steps were of shorter duration and had slightly lower peak toe elevation and velocity. Difference in vertical toe position at obstacle contact (0.08 m for T-FZ trials and 0.04 m for T trials) disappeared around 200 ms after contact and reversed to a maximum contrast around 400 ms after obstacle contact. At this time the vertical toe position was 0.05 m for T-FZ trials and 0.18 m for T trials, in line with the fact that the average T-FZ landing occurred around 410 ms, while recovery steps during the T trials lasted longer and landed around 480 ms. The same pattern was seen for vertical toe velocity; following a difference at obstacle contact (-0.1 m/s for T-FZ trials and -0.3 m/s for T trials), the velocities became equal around 80 ms after obstacle contact, reversed around 120 ms and reached a maximum contrast around 320 ms after obstacle contact (-1.9 m/s for T-FZ trials and -0.8 m/s for T trials). In other words, subject started lowering their foot about 20 ms earlier during the T-FZ trials (vertical position of the toe started decreasing around 280 ms during the T trials and 260 ms during the T-FZ trials), which was preceded by a slowing down of the vertical toe velocity occurring about 60 ms earlier (T trials 220 ms, T-FZ trials 200 ms). In combination with a difference in peak toe position (T trials 0.32 m, T-FZ trials 0.28 m) this led to landing about 70 ms earlier during the T-FZ trials.

In terms of muscle activity, earlier lowering of the foot was expected to require additional activity in extensors (iGM as plantar flexor and iBF as hip extensor) and a reduction of activity in flexors (such as iTA). Such activity changes indeed occurred, but not in the early phase of the recovery reaction. Changes in iGM activity started on average 107 ms following trip onset with reduced (rather than increased) activity during T-FZ trials. This reduction reached its maximum around 146 ms after trip onset (T-FZ trials 0.42 and T trials 1.83) and was followed by a period of increased activity starting at 267 ms and reaching a maximum at 323 ms (T-FZ trials 1.50 and T trials 0.14 times normal walking activity) after trip onset. The second muscle to show a change in activity was iTA, which activity was reduced during the T-FZ trials. In iTA, the earliest change was found at 171 ms after trip onset. This initial reduction in activity reached its maximum 225 ms following trip onset (T-FZ trials 0.34 and T trials 1.37 times normal walking) and was followed by another period of reduction starting at 329 ms and reaching its peak 450 ms after trip onset (T-FZ trials 0.26 and T trials 0.82 times normal walking). Note that the recovery foot landing occurred around 410 ms during the T-FZ and 480 ms during the T trials. The third muscle to be activated differently between T and T-FZ trials was iBF. Excitation of iBF started

235 ms and reached a peak at 285 ms (T-FZ trials 1.73 and T trials 0.32 times normal walking) after trip onset. Finally, the only significant change in RF activity occurred much later, around 480 ms following obstacle contact, when the recovery steps were already completed.

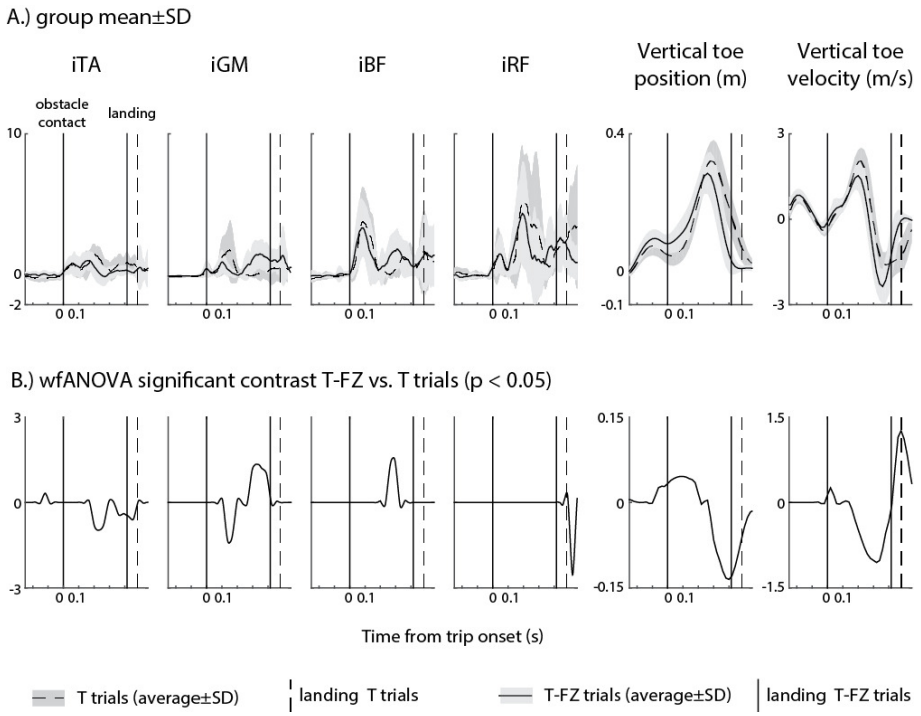

Figure 6.5. Group average responses (A) and significant contrasts (B) between normal trips (T) and trips with a FZ (T-FZ), for the ipsilateral leg. Group average data are shown as mean ± standard deviation. All signals are aligned to obstacle contact, indicated by a black vertical line at time = 0. Other vertical lines indicate recovery step landing for T (dashed line) and T-FZ (solid line) trials. EMG data are normalized to average normal walking and thus unitless. Contrasts are expressed in the same way, since they represent the difference in normalized EMG data between T-FZ and T trials.

The comparison between T-FZ and TC trials yielded no statistically significant contrast. However, TC trials significantly differed from T trials in many aspects, although the perturbation was the same (trip without the FZ) in both of these trial types (T and TC). As can be seen in Figure 6.6, these differences were similar to the difference between the T and T-FZ trials. Difference in vertical toe position at obstacle contact (0.08 m for TC trials and 0.04 m for T trials) disappeared around 220 ms after contact and reversed to a maximum contrast around 380 ms after obstacle contact (0.1 m for TC trials and 0.22 m for T trials). Vertical toe velocities

were equal at obstacle contact and reached a maximum contrast around 280 ms after obstacle contact (-0.5 m/s for TC trials and 0.6 m/s for T trials). Overall the behavior during the TC trials was similar to that during the T-FZ trials: subject started lowering their foot about 20 ms earlier (vertical position of the toe started decreasing around 280 ms during the T trials and 260 ms during the TC trials), preceded by a decrease in the vertical toe velocity about 60 ms earlier (T trials 220 ms, TC trials 200 ms). Peak vertical toe position was 0.32 m during the T trials and 0.30 m during the TC trials and the TC steps landed about 50 ms earlier.

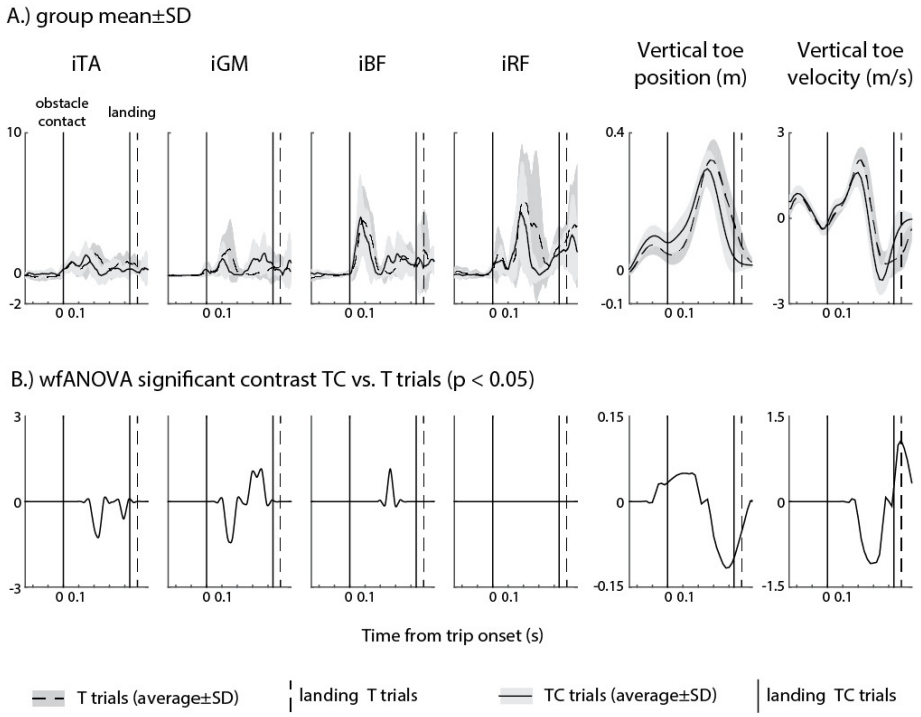

Figure 6.6. Group average responses (A) and significant contrasts (B) between normal (T) and 'catch' trips (TC), for the ipsilateral leg. Group average data are shown as mean ± standard deviation. All signals are aligned to obstacle contact, indicated by a black vertical line at time = 0. Other vertical lines indicate recovery step landing for T (dashed line) and TC (solid line) trials. EMG data are normalized to average normal walking and thus unitless. Contrasts are expressed in the same way, since they represent the difference in normalized EMG data between TC and T trials.

Muscle activities of the TC trial also differed from the T trials and were similar to activities seen during the T-FZ trials. As for T-FZ trials, the earliest change was found in iGM. The reduction in iGM activity started at 107 ms and reached a peak 156 ms after obstacle contact (TC trials 0.24 and T trials 1.76 times normal walking), before

reversing to an excitation starting 267 ms and reaching a peak 356 ms (TC trials 1.16 and T trials 0.27 times normal walking) following obstacle contact. The second muscle to show a change in activity compared to the T trials was iTA, with a reduction in activity starting 171 ms after obstacle contact and reaching a peak at 225 ms after obstacle contact (TC trials 0.23 and T trials 1.37 times normal walking). This was followed by another period of reduction starting at 364 ms and reaching its peak at 392 ms after obstacle contact (TC trials 0.29 and T trials 0.79 times normal walking). Finally, activation of iBF started at 236 ms and reached its peak at 264 ms after obstacle contact (TC trials 1.16 and T trials 0.13 times normal walking).

Foot kinematics

Since significant contrasts were mainly found in iGM and iTA muscles, which serve as ankle plantar- and dorsiflexors, respectively, we evaluated the position of the foot throughout the recovery step. Given the increased iGM activation along with reduced iTA activity during the T-FZ and TC trials, one would expect that in these trials the foot would land with a toe landing (i.e., in plantar flexion). This was confirmed by the data. Subject and group averaged foot position curves are shown in Figure 6.7, based on the vertical distance between toe and heel with a positive difference indicating heel landing (toes up or dorsiflexion). It can be seen that the recovery foot was constantly in plantarflexion during T-FZ and TC trials and subjects ended the recovery step by landing on their toes, which were, at landing, 0.11 m below the heel during the T-FZ trials and 0.07 m below the heel during TC trials. In contrast, during the T trials the subjects had the toes 0.01 m above the heel, indicative of a flat foot landing.

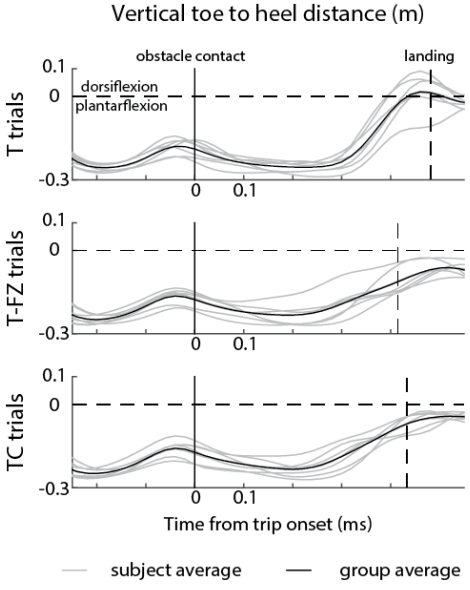

Figure 6.7. Vertical distance from toe to heel for T, T-FZ, and TC trials. Subjects' average data are shown in grey and group average is shown in black. Signals are aligned to obstacle contact, indicated by a black vertical line at time = 0. Vertical dashed lines indicate recovery step landing. Note that positive vertical distance indicates upward direction. Thus, positive distance between the toe and the heel at landing indicates heel landing (i.e., dorsiflexion), while the negative distance indicates toe landing (i.e., plantarflexion).

Discussion

This paper aimed at exploring the mechanisms involved in making decisions related to fast leg movement adjustments under balance threatening conditions, namely changing the landing position after tripping (in order to avoid stepping in a "forbidden landing zone"). In a previous study on the same data, we had shown that such corrections can be made in a large percentage of the trials. However, since the EMG data were not yet provided, decisions underlying such fast corrections remained unknown. In the present study we addressed this issue by describing muscle activity changes driving leg movement adjustments and showed that the correction to avoid the FZ after tripping clearly involved a two-stage process: the first stage of the response was seemingly unrelated to the behavioral outcome whereas the second, later stage of the response consisted of muscle activity changes needed to initiate the observed step shortening.

Behaviorally, the response to the FZ analyzed in this study was step shortening, which means the foot was placed in front of the FZ, hence requiring an earlier landing of the foot. One would predict that this requires additional activation of hip extensors (iBF) and ankle plantar flexors (iGM), along with suppression of dorsiflexors (iTA). This was indeed observed; the reduction in iTA activity occurred first (171 ms) and was followed by activations in iBF and iGM at relatively long latencies (235 and 265 ms, respectively). Surprisingly, the functional activation of iGM was preceded by a period of reduced (instead of increased) iGM activity starting at a latency of 107 ms. Hence the total response had two stages: it started with a nonfunctional change in iGM muscle activity and was followed by a functional activity changes in iTA, iBF, and iGM, which occurred at longer latencies and led to step shortening.

To understand this two stage decision making process, it is essential to first consider what is known about the neurophysiology of tripping. In a previous study on tripping it was shown that tripping induces a series of responses with different latencies [78, 161]. Two of these responses had latencies below 100 ms. The earliest responses (~40 ms) were identified as stretch reflexes and were followed (~75 ms) by medium latency cutaneous and proprioceptive responses. Both responses did not determine the behavioral response strategy since the latter depended only on responses occurring with a latency of about 110 ms [78, 81]. These types of responses were identified in the present study as well, but superimposed were two additional responses, related to the movement correction caused by the real or expected appearance of the FZ. These additional responses went along the same lines as described before, namely one initiated at a latency below 150 ms (the limit for

"involuntary reactions"), followed by longer latency muscle activity changes appropriate for the behavioral response (i.e., step shortening).

Finally, we evaluated the influence of anticipation on this decision making process by analyzing performance on TC trials, which required no movement adjustment. Anticipation influenced subjects' behavior and they shortened their steps even when the FZ was not shown, using similar movement adjustment mechanisms as used for the T-FZ trials. Since anticipation influenced the performance on TC trials it also probably influenced the T-FZ trials. However, this influence of anticipation did not fundamentally change the process by which movement adjustments occurred and the performance on the first trial requiring movement adjustment was similar to the performance on the ensuing trials.

The first stage: early suppressive responses

The most puzzling new feature, seen in the present study, was the reduction of normal trip recovery iGM activity, starting at ~100 ms after trip onset in T-FZ and TC trials. A first explanation could be that this reduced activity was related to the increased dorsiflexion and foot clearance at trip onset, reflecting a learning effect over trials. T trials were executed first and subjects might thus have adjusted their normal gait to make it easier to overcome the obstacle during the subsequent T-FZ and TC trials. The reduced iGM activity would fit the dorsiflexion hypothesis, but it is puzzling that it appears only after a latency of about 100 ms. Furthermore it is not accompanied by a clear deflection in the foot trajectory at a latency compatible with the electromechanical delay (at 200 ms after obstacle contact the foot was only slightly more dorsiflexed during the T-FZ and TC trials). Additionally, the averaged data of individual subjects showed that the combination of increased dorsiflexion and reduced iGM activity was present only in four out of seven participants. The remaining participants exhibited reduced iGM activity in combination with plantar flexion or, in one case, increased iGM activity in combination with dorsiflexion. Together with the fact that there was no concomitant increase in iTA activation and that the reduced iGM activity was present in both TC and T-FZ trials, this indicates that the reduction in iGM activity was not a functional response enabling dorsiflexion.

A second possible explanation is that the reduction of iGM activity is related to the presence of a real or expected FZ. This reduction occurred at a latency which was too short to be consistent with a voluntary reaction (<150 ms) and was not solely dependent on anticipation of the FZ, since it was present already in the first T-FZ trial in four out of seven participants.

Although only observed in iGM, the reduced activity could represent a suppression of activity. Such hypothetical suppression could be seen as part of a "freeze" or

"pause" response, giving the system appropriate time to prepare an adequate reaction (shortened step). In animals, including humans, it is common to see a freezing reaction as part of a defensive response strategy followed by appropriate reactions such as fleeing or fighting back in case of a real danger [166]. Such suppression appears when unexpected startling stimuli are presented. For example, pronounced muscle activity suppression was found in response to a loud noise during gait with a latency of ~100 ms [162, 167]. Sometimes the freeze is also accompanied by a cocontraction of agonists and antagonists (producing joint stiffening, [162]), but this was not observed in the present study. The precise pathway involved in the suppressive responses is still unclear, but it is striking that loud acoustic stimuli can evoke suppression in the motor cortex as well, implying that a long loop over the cortex is a possibility [168–171]. The currently observed presumed suppressions were time locked to the onset of tripping, hence one could argue that the sound of the contact with the obstacle contributed to the startling "freeze". However, this sound was also present during normal tripping, indicating sound was not the determining factor. It is clear that the triggering of the response was not purely visual either, since suppression of normal walking activity was not seen during FZ trials. Hence, the brief presumed suppressions in iGM seem to be triggered by the combination of tripping and the need for step adjustment, either real or expected. In this respect, it is useful to recall that other stimuli can produce similar inhibitory effects. For example, for unexpected somatosensory stimuli such suppressions have also been noted. With stimulation of cutaneous afferents from the foot, suppression of muscle activity has often been observed (for example in TA and triceps surae muscles), with latencies in the range of 50-100 ms [172–175]. Again however, such stimuli could not have been the sole source for the observed suppression here since somatosensory stimuli were the same for all tripping trials. While the origin of this reduction in iGM activity remains unclear, such decreased activity could not contribute to step shortening and it therefore does not belong functionally to the muscle activity changes occurring at longer latencies, which all clearly could contribute to step shortening.

The second stage: behavioral responses (shortening strategy)

Following the early suppression response ("freeze" period), EMG changes were clearly related to step shortening in order to avoid the FZ, i.e. rapid lowering and placement of the tripped foot in front of the FZ, once it had cleared the obstacle. The facilitations of iBF (at 285 ms) and iGM (at 320 ms), along with the suppression of iTA (at 171 ms) are consistent with shortening of the step and plantarflexion in order to prematurely lower the leg and land on the toes (Figure 6.7). It is interesting to note that the latencies of movement adjustments in response to the FZ, as seen here, correspond to those reported for the hamstrings and plantarflexors in a trial in which the tripped subject started with an elevating strategy and switched to lowering due

to an obstacle sticking to the foot ('delayed lowering') (Figure 6 in [78]) and to latencies of differences in muscle activity between elevating and lowering trip recovery strategies [81].

Online adjustment or anticipation?

One of the problems with studies using repeated perturbations is that only the very first perturbation trial is truly unexpected and that upcoming perturbations can influence the recovery stepping response [176] and alter the normal walking pattern [154, 157]. When anticipating a trip, young subjects increase their step width and exhibit small changes in muscle activity that lead to knee stiffening, dorsiflexion and increased foot clearance. This has led some authors to limit their study to only one unexpected tripping trial for each subject [143, 176, 177]. In order to address this issue, we included a number of catch trip trials in our experimental design. These trials differed only in that the catch trials were presented in between the T-FZ trials, while normal trip trials occurred at the start of the experiment, before any FZ was presented. Yet, we found the performance to differ between these trial types. Behavioral changes on the TC trials were similar to those on the T-FZ trials, but of smaller magnitude. Steps were shortened both in time and distance and in nine out of fourteen trials included in this analysis would even have landed outside of the FZ, if it had been presented (see also [131]. Muscle activity changed accordingly, showing a similar pattern of decreased iGM and iTA activity, followed by an increase in iBF and iGM activity. This clearly showed that anticipation was involved in the catch responses. Apparently, when faced with the possibility of encountering the FZ, the subjects' responses were suitable for that situation even if no FZ was present. This behavior might be related to the co-optimization of motor behavior such that an anticipated FZ could be more easily avoided if shown [178]. Since anticipation affected the performance on catch trials it was also likely to affect most T-FZ trials. The only exception was the very first T-FZ trial, in which subjects had no prior experience of the adjustment required.

To see the signature of a true adjustment of a balance recovery response, we looked at the very first trial with a FZ, since this is the trial in which the reaction was based on visual input mainly and not (or to a much lesser extent) on anticipation. If the influence of anticipation would be important, we would expect large changes in responses over the subsequent trials. However, the data showed that the response pattern did not differ much between the first and subsequent trials, the only observed change was a decrease in the magnitude of activity of some muscles (e.g., iRF), in line with previous work suggesting amplitude decrease with habituation [179, 180]. This is relevant for the question whether the responses seen in the first trial are basically different from the subsequent ones or whether they are the same, but that there is mostly a scaling difference. This type of question has been investigated most thoroughly with postural perturbations [179, 180] and it was found that first

trial responses definitely show characteristics of startle responses. However, they also differ from startle responses in some aspects and it was therefore concluded that first trial effects are likely postural responses which are superimposed on a startle response [179]. Our experiment was somewhat different, since our subjects were already tripped before the first T-FZ trial. In the T-FZ trial, the visual stimulus was added to the trip, but this would presumably cause less of a startle than a novel balance perturbation. Therefore it is not surprising that responses to the T-FZ trials exhibited a modest amplitude scaling, but not a major new pattern in the first trial.

Muscle activity during normal trip recovery

Since muscle activity was also recorded during normal tripping, we compared our data with those obtained in former studies on tripping responses. Muscle activity used for recovery steps during normal tripping in the present experiment was generally similar to that reported previously for elevating response recoveries from trips during overground [85] and treadmill walking [78, 161]. Amplitude peaks first occurred in iBF (~80 ms), followed by iGM (~150 ms), iTA (~205 ms), and iRF (~195 ms), similar to previous findings either on a treadmill [78] or overground [85]. Furthermore, similar to Schillings et al. [161] we occasionally measured very early responses to the tripping perturbation in iTA (~60 ms) and iRF (~40 ms). The main difference with these previous studies was the long latency of the late iGM activity. Such activity was either not measured [79, 85] or not found to be significant previously [78]. This large and late iGM activation might play an important role in trip recovery, when the obstacle is high and does not move (in contrast to the Schillings et al. studies). Indeed, higher foot elevation has to be compensated by increased plantar flexion at landing.

Limitations

One limitation of this work lies in the fact that it was technically impossible to achieve exactly identical tripping onsets during the swing phase in all trials. As shown earlier [154, 157], subjects change their gait pattern when expecting a potential perturbation and this is a limiting factor for these types of experiments. Although we encouraged our subjects to maintain their normal gait pattern and walking velocity and presented them with a number of normal walking trials in between the tripping trials, vertical toe position and velocity already differed slightly between the T and T-FZ trials at trip onset, because the T trials were performed earlier than T-FZ trials (see also [131]. Nevertheless, as mentioned in methods the tripping always elicited a balance recovery response with an elevating strategy. Finally, we are limited in sample size, as only seven (out of sixteen) subjects tested exhibited consistent behavior (i.e., successfully avoided the FZ using the same strategy in each trial).

Conclusion

In line with the findings that tripping induces muscle activity responses at different latencies and only the longer latency responses are related to the balance recovery responses (elevation or lowering; Schillings et al., 2000), we found that adjustments of these recovery responses (to avoid a forbidden landing zone) also involve two stages in the decision process. The first response (decrease in iGM activity at around 100 ms after trip onset) occurred too early to be voluntary (<150 ms) and might reflect a temporary "pause", enabling the system to collect information for the ensuing behavioral response. Behaviorally functional EMG responses occurred later (>230 ms) and led to appropriate movements to avoid the forbidden landing zone, in this case by shortening the recovery step. Interestingly, anticipation of the potential need for movement adjustment led to similar two-stage responses even when no forbidden zone was present during tripping.

Acknowledgements

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7 GENERAL DISCUSSION

In this thesis, the ability to adjust leg movements during balance challenging situations of unobstructed and obstructed gait was investigated and the underlying mechanisms were explored. Studies investigating leg movement adjustments from a non-clinical point of view are relatively few and often involve step initiation, hence the need for the present work. While step initiation is an easy way to use paradigms borrowed from the more advanced field of arm movement adjustment research, it is not fully representative of daily life circumstances of falls [11], one of the direst consequences of unsuccessful adjustments of leg movements during gait.

Therefore, the work presented in this thesis focused on the ability to modify foot landing position of an ongoing step during precision gait (part one) and during balance recovery following tripping (part two). Both situations pose considerable balance constraints, which might influence the ability to adjust ongoing leg movement. Furthermore, these situations more closely reflect common daily life circumstances in which leg movement adjustments are needed and thus add ecological validity and clinical relevance to this work, besides addressing the fundamental issues of fast control of leg movement adjustments.

Part 1: step adjustment during precision gait

In the first part of the thesis (Chapters 2 to 4) we used a set-up comprising of an instrumented treadmill and a generic projector to project visual stepping stones on the treadmill and asked our subjects to walk by stepping on these stepping stones. This precision stepping during gait was then used as a basis for two types of step adjustments: one based on the stop-signal paradigm, requiring avoidance of stepping stones suddenly turning into obstacles (Chapters 2 and 3), and the other based on the double-step paradigm, forcing the subjects to follow stepping stones that suddenly shifted position (Chapter 4).

Our first study, presented in Chapter 2, focused on the development of a novel walking task based on the stop-signal paradigm, which stressed the inhibitory requirements of obstacle avoidance. In this task subjects were required to adjust their ongoing precision gait in response to a sudden change in the color of an approaching stepping stone. This change of stepping stone color indicated it became an obstacle to avoid. To be able to avoid the colored stepping stone, subjects first had to inhibit their ongoing step. Thus the task was named precision step inhibition (PSI) task. We expected that stressing motor inhibition during precision gait would produce more failures compared to conventional obstacle avoidance protocols and we tested the performance of young adults (YA) at various task difficulty levels in order to establish a protocol for use in older adults (OA).

During pilot experiments the PSI task proved challenging even for healthy young adults and often lead to discouragement and frustration if performed unsuccessfully.

Therefore, we decided on a testing protocol that used individualized difficulty levels based on task practice. As expected, we observed an increase in failure rates with increasing task difficulty, demonstrating this test is a sensitive measure of response inhibition during obstacle avoidance. Furthermore, we found increased failure rates compared to previous obstacle avoidance studies [5, 57, 64, 65], indicating the PSI task is more challenging than previously used obstacle avoidance tasks.

After establishing a feasible testing protocol we tested PSI task performance of older adults and these findings are reported in Chapter 3. As expected, the performance of older adults was worse than the performance of young adults, both at equal absolute levels of difficulty and when comparing individualized difficulty levels. These findings are consistent with previous experiments reporting deteriorated ability of older adults to adjust leg movements during step initiation [7, 53], walking [8] and obstacle avoidance [5, 6, 10, 65]. As in the previous chapter for young adults, failure rates of older adults were higher compared to previous obstacle avoidance studies [5, 57, 64, 65], probably reflecting the increased complexity of the PSI task. However, while young adults demonstrated increased failure rates with increasing PSI task difficulty, older adults showed a strong learning effect and improved their performance with time. While this limited our conclusions, it seems promising for fall prevention.

Aside from evaluating single task performance on the PSI task, we wanted to investigate to what extent the PSI task involved cognitive loading. To address this issue we paired the PSI task with a cognitive task that occasionally required response inhibition and had older and young adults perform the two in a dual task setting. Our expectation was that performing the two tasks simultaneously would affect performance only if the PSI task posed cognitive demands. An additional question we wanted to address was whether the PSI task required response inhibition specifically. If this was the case, dual task interference would be more prominent when the cognitive task also required inhibition. For the cognitive task we chose a Stroop task in which subjects were supposed to verbally respond to congruent or incongruent auditory stimuli. Both types of stimuli pose cognitive demands, but only incongruent stimuli require response inhibition to respond correctly. Thus, analyzing the difference in performance between congruent and incongruent stimuli provides insight into inhibitory requirements of the two tasks and the capacities of our subjects. Our expectation was that both tasks would require inhibition, which was indeed the case. Performance on the Stroop task was worse in response to incongruent stimuli and, importantly, we could see that congruence of the Stroop stimuli affected the rate of incorrect responses of young adults only when obstacles were added to precision stepping, indicating inhibitory requirements of the PSI task. Finally, in line with previous studies we found deteriorated inhibitory abilities in older adults [98, 99] and dual task interference [10], confirming that response

inhibition under time pressure is global [28, 110]. With respect to dual task interference, older adults prioritized the PSI task, but young adults did not.

Additionally, to confirm the link between response inhibition and the PSI task, we analyzed the performance of young and older adults on a computer task of response inhibition, which required inhibition of hand movements (adapted from [28]) and correlated it to their performance on the PSI task. While these data form a basis for additional investigation, it is possible to show the preliminary results here (Figure 7.1).

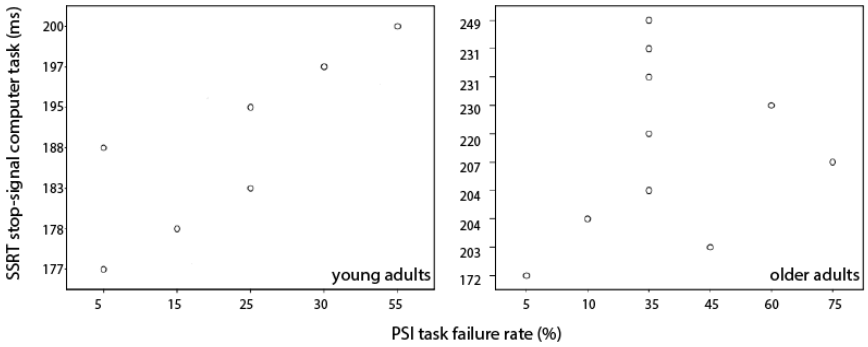

Figure 7.1. Performance of young (left) and older adults (right) on a computer task of response inhibition compared to their performance on the PSI task. Performance on the computer task is expressed as stop signal response time (SSRT, the lower the better, in ms) and performance on the PSI task is expressed as percentage of failures. The PSI task was performed as a single task and difficulty was set to an available response distance (see Chapter 3) of 500 mm.

Specifically, we used Spearman correlation to correlate the stop signal response time (SSRT), a common measure of response inhibition in the stop-signal paradigm, with the failure rates on the PSI task for 10 older and 7 young adults in which the individually tailored PSI task difficulty level overlapped at an available response distance (ARD) of 500 mm. As can be seen in Figure 7.1, we found a strong correlation between inhibitory performance on the computer task and the PSI task performance of young (r_s =0.818, p = 0.02), but not older adults (r_s =0.176 , p = 0.5) [30].

These data, taken together with Chapters 2 and 3, indicate response inhibition is important for leg movement adjustments during obstacle avoidance.

Once the ongoing step is stopped, an alternative foot landing must be found among various possible positions. Most often people, both young and older adults, either lengthen or shorten their steps [1, 5, 9, 57, 59, 61, 64, 69, 70], but what drives this decision is not clear. We wondered whether different ways in which obstacles could be avoided are related to the ability to execute specific step adjustments. For

example, when time pressure is low subjects typically prefer to lengthen their ongoing step to avoid an obstacle [9, 64]. Could this be because lengthening a step is more accurate and thus chances for a successful movement adjustment are higher? Accuracy of movement adjustment could not be evaluated using our PSI task, since subjects were free to position their foot anywhere but on the stepping stone that turned into an obstacle. Therefore, in Chapter 4 we took a different approach in order to address this question. Instead of building our experimental task on the stop-signal paradigm and forcing subjects to avoid obstacles, we used the double-step paradigm and forced them to land on a stepping target that could shift position. Namely, subjects had to adjust their precision stepping to follow stepping stones that could shift in the forward, backward, or lateral direction during approach. Since we knew what kind of movement adjustment was required, we evaluated the accuracy of the executed adjustment by comparing the foot landing position with the shifted stepping stone position. This way we could evaluate the ability to execute specific movement adjustments, and not the ability to execute a movement adjustment chosen freely from an array of possibilities, as is the case during obstacle avoidance. We suspected that the direction of movement adjustment might influence its accuracy [66] and this was indeed confirmed by the data. Young adults performed step lengthening more accurately and successfully than shortening or stepping to the side; the latter two did not differ significantly, but step shortening was slightly less successful than side stepping. Given these differences in the ability, it is clear that step lengthening comes with the lowest risk of unsuccessful obstacle avoidance, which might be an underlying reason for the step lengthening preference observed in previous obstacle avoidance studies [9, 64, 69]. However, if this is the case, why would step shortening be used at all? Our data show that the difference in accuracy between step lengthening and shortening gets smaller with increasing time pressure. On the other hand, it was proposed that the metabolic cost might be higher for step lengthening compared to shortening [9]. If this is the case and failure rates of the two strategies are comparable under the given circumstances, step shortening might become beneficial.

Part 2: step adjustments during trip recovery

In the second part of this thesis we focused on leg movement adjustments following tripping, which is even more challenging in terms of balance. We wondered whether it is possible, and if so, how, to adjust trip recovery steps, which are already gait adjustments in order to regain balance. That such adjustments would be possible was not immediately predictable and, because of high demands to regain balance under time pressure, it is conceivable that these recovery steps are ballistic reactions, not allowing feedback corrections [93]. In order to address this issue we unexpectedly tripped young adults during overground walking and presented them

with a forbidden landing zone (FZ) at trip onset. The FZ was located at their preferred trip recovery step landing position and, in order to avoid it, subjects had to quickly adjust their leg trajectory while regaining balance.

As presented in Chapter 5, we found young adults were able to adjust their trip recovery steps, although individual differences in success rates were evident. Some subjects succeeded already in their first FZ trial, while others took longer and were successful only in the final, fifth trial. However, all subjects succeeded at least once and none lost balance. Although leg trajectory adjustment attempts, both successful and unsuccessful, caused changes in angular momenta, these changes were small and did not threaten trip recovery.

Our results showed that adjustments were possible and successful avoidance was observed already in the first trial in 60% of the subjects. Since the FZ was in fact an obstacle to be avoided during balance recovery, we were also interested in strategies used for its avoidance. Unlike obstacle avoidance during gait [9, 64], step shortening was the predominant strategy for FZ avoidance during tripping. It was used in 84.2% of all successful trials, while the remaining trials utilized stepping to the side of the FZ. Strategy selection was related to subject's height: taller subjects used step shortening, while shorter subjects used side stepping, probably due to a smaller distance between the tripping obstacle and the FZ. Namely, the FZ was positioned based on the subject's normal trip recovery steps, which were shorter in shorter subjects. Surprisingly, no step lengthening was used, although it might be beneficial in terms of time, angular momentum, and accuracy of movement adjustment. However, our FZ was quite large (50 cm long and 30 cm wide) in order to ensure each step outside of the FZ is the result of a movement adjustment. Such large size of the FZ was the likely cause of the observed preference for step shortening, as it made step lengthening too challenging.

One of the striking findings presented in Chapter 5 was the observed learning effect. FZ avoidance success rates significantly improved over trials, from 60% in the first trial to a 100% in the fifth, final trial. This learning effect was also evident in the performance on two normal 'catch' trip trials that occurred in between the FZ trips. Although no FZ was presented on these trials, subjects adjusted their steps and landed further away from the FZ than during normal tripping, which occurred prior to any FZ presentation. Apparently, anticipation of a possible FZ affected the tripping response even if the FZ did not appear.

In the Chapter 6 of this thesis we explored the mechanism underlying leg movement adjustments during trip recovery. We focused on trip recovery step shortening, the dominant strategy used for FZ avoidance, and analyzed the concomitant muscle activity changes. Our data indicated that muscle activity changes involved two distinct stages. The first stage was not related to the observed behavior (i.e., did not

help to shorten the step) and started at a latency shorter than voluntary reaction time. The second stage involved muscle activity changes contributing to the observed behavior and started at latencies corresponding to voluntary reactions. Specifically, the first stage of the response consisted of an absence of muscle activity at a time that this was expected. This absence of activity was observed only in gastrocnemius medialis, was not functional and started around 100 ms following trip onset. The second stage response started around 170 ms following trip onset and consisted of a functional reduction in activity of tibialis anterior and increase in activity of biceps femoris and gastrocnemius medialis, which led to step shortening and landing on the toes. Strikingly, we found similar muscle activity changes and adjusted steps during 'catch' trials of normal tripping, although they did not involve a FZ.

The first stage of the response, reduced gastrocnemius medialis activity, was difficult to explain, since it was not related to the observed change in behavior. It was present in the first FZ trial in four out of seven participants, indicating it is not dependent on anticipation of the FZ. However, it was also seen during 'catch' trials, when no FZ was present. Although such non-functional muscle activity change was only observed in one muscle, we suspect that it might have been a part of a 'freeze' or 'pause' response triggered by a combination of tripping and the need (real or anticipated) for step adjustment. As such it could provide time before an appropriate reaction is initiated, but its origin remains unclear. The second stage of the response was much easier to explain, since the observed changes in muscle activity led to step shortening and landing on the toes. Finally, it is interesting to note that the latency at which the second stage response started was similar to latencies at which muscle activity starts to differ between different strategies used for recovery during normal tripping [78, 81].

In line with findings reported in Chapter 5, during 'catch' trip trials our subjects exhibited behavioral and muscle activity changes similar to those seen on trials with a FZ. This indicates leg movement adjustments during tripping occur under the influence of anticipation, irrespective of the actual need for a movement adjustment. Since there was no cost associated with an unnecessary movement adjustment, subjects might be co-optimizing their motor behavior to facilitate avoidance of the FZ, if it occurs [178]. Under these circumstances, it is reasonable to assume anticipation also affects the performance on the FZ trials. We inspected the muscle activity response patterns and found little change between the first and subsequent FZ trials. The only observable change was a slight amplitude scaling, possibly due to habituation [179, 180]. Thus, this method was able to induce online movement adjustments already in the first trial and these exhibited a similar muscle activity pattern as movement adjustments on subsequent trials, which presumably relied on a mixture of anticipation and online adjustments.

Comparisons to arm movement adjustments

Our work shows it is possible to study leg movement adjustments using paradigms from arm movement research adapted to gait. However, it is important to note that biomechanical constraints and physical ability to execute a specific adjustment might influence the performance on leg adjustment tasks to a greater extent. Nevertheless, both the stop signal and double step paradigm tasks that we adapted to gait were successfully performed by our subjects, and some similarities with the findings from arm movement adjustment field exist.

Most importantly, with respect to response inhibition, our findings presented in Chapters 2, 3, and 4, as well as previous studies [5–8, 52, 53, 57, 61, 64, 65, 69, 70] show that the ability to adjust steps in order to follow shifting stepping targets or avoid obstacles decreases with a reduction in time available to complete these adjustments. This is in line with the proposed race model of response inhibition in which a response is inhibited only if the 'stop' process finishes before the 'go' process. Hence, if one receives the 'stop' signal (a stepping target shift or appearance of an obstacle) too late, stopping the ongoing movement is impossible. Furthermore, learning and anticipation effects observed in our PSI and tripping experiments are reminiscent of the behavior typically exhibited by subjects performing stop-signal tasks for the arms [26, 29]. Namely, a change towards more cautious behavior seems to occur both for leg (Chapters 5 and 6) and arm movements [24] following stop signal perturbations and, more generally, for leg movements following balance perturbations [87, 151, 154, 157]. Finally, with respect to age and the deteriorated ability to perform the PSI task (Chapter 3) and step adjustments in general [5–9, 52, 53, 65], it is interesting to note that the ability to walk successfully, i.e., without falling seems to be related to deterioration of executive function (and response inhibition as its component) [43–48]. In general, executive function is associated with the frontal cortex (see Appendix for a detailed description of neural correlates of response inhibition) and deteriorates with aging [40–43]. While research on neural correlates of arm movement adjustments is abundant (see Appendix), neural correlates of leg movement adjustments are not known. However, research linking age related gait stability deterioration to changes in white matter integrity in tracts connecting subcortical and prefrontal areas [181] is in line with structures proposed as neural correlates of arm movement adjustments (see Appendix).

Methodological considerations

Several limitations of the studies presented in this thesis should be addressed.

In Chapters 2 and 3 we tested the PSI task performance of young and older adults using a protocol consisting of four increasing difficulty levels, which were individually adjusted based on initial ability. We opted for such a protocol because of the

frustration and discouragement observed when our subjects were not able to perform the task at given ARDs during pilot experiments. However, this could have resulted in fatigue and learning effects. Fatigue effects would have led to more failures in the later condition, while learning effects would have the opposite effect. Neither was the case in young adults, but a learning effect occurred in older adults. Although older adults initially performed poorly, it seems that with more training they might be able to perform the PSI task at more difficult levels. This limits our ability to address the magnitude of age related deterioration in PSI task performance, for which an additional study is currently underway. With respect to Chapter 3, an additional limitation of the experiment was our inability to synchronize the Stroop task stimuli to obstacle presentation in the PSI task. However, our conclusions were drawn carefully and these limitations should not influence them.

In Chapter 4 we evaluated the ability to execute movement adjustments in the forward, backward, and lateral direction, but unfortunately could not measure the ability to execute medial movement adjustments. Namely, we used a dual belt treadmill and, in case of medial movement adjustments, our subjects could have been perturbed by the gap between the two belts of the treadmill. Medial adjustments are rarely used for obstacle avoidance, but could be of interest, because they threaten balance more than lateral adjustments. If possible, future research should include these as well.

With respect to our experiment on tripping presented in the second part of this thesis, an important factor to consider is that it was impossible to achieve exactly identical tripping onsets in all trials. It is known that subjects change their gait pattern [154, 157, 176] when anticipating a potential perturbation and this is a limiting factor for perturbation experiments. One of the ways this issue can be tackled is to avoid perturbing the same subject multiple times. However, this repetition was needed in our experiment in order to compare subjects' responses to trips with and without the FZ. Therefore, we tried to minimize anticipatory changes in the gait pattern by encouraging our subjects to maintain gait pattern and walking velocity as shown at the beginning of the experiment. Furthermore, we included a random number of normal walking trials in between the tripping trials, to 'wash-out' the anticipation and ensure unpredictability of tripping. While we did see some minor kinematic changes between different trip trials, we believe these changes were not to the extent that our conclusions are invalid. Additionally, our analyses of muscle changes underlying step shortening for FZ avoidance presented in Chapter 6 were limited by the sample size. Only seven (out of sixteen) subjects tested exhibited consistent behavior and used the same strategy (step shortening) to successfully avoid the FZ in all trials.

Finally, all of the presented studies used projections of light to trigger movement adjustments. While this approach is highly promising, since it enables more flexibility

in the way obstacles and targets are presented by triggering visual context based on online data of subjects' behavior, it is limited by the difficulties of measuring the appearance of light. Namely, previous research could e.g., equip physical obstacles with kinematic markers and use the same measurement system to measure the behavior of the subject, the obstacle, and their interaction. This, of course, is not possible with virtual obstacles and targets. Using a novel approach proved challenging in these studies, especially since we were relying on a clinical system for precision stepping adjustment experiments. Specifically, in the experiment presented in Chapters 2 and 3 we could not precisely synchronize the appearance of a color change in the visual context to kinematics of the behavior and had to rely on a video analysis of the PSI task performance, which was time consuming and limited in the level of detail it provided. In the remaining experiments it was possible to synchronize various systems used for measurement and visual context projection, but while we knew when the change in visual context was triggered to appear we could not measure its appearance precisely in each trial. If we were able to do so, our analyses might be easier and more precise. However, these technical difficulties should not discourage future work.

Future directions for research and clinical use

The work presented here could be extended in several meaningful ways. First of all, this thesis focused on the swing leg, whose trajectory was being adjusted. However, the contralateral support leg certainly contributes in executing movement adjustments, as it does during trip recovery [80, 91] and step initiation [37, 182], and future work would benefit from the analysis of its muscle activity and kinematics. Additionally, since balance requirements might be a factor limiting performance or willingness of humans to execute leg movement adjustments [5, 9, 50, 55, 63, 84], future work would benefit from quantifying stability [96] and investigating its influence on movement adjustment execution.

The PSI task we developed to assess the role of response inhibition seems a promising tool for future research. While we reported age deteriorated ability to perform the PSI task, we could not address the magnitude of this deterioration due to learning effects observed in older adults. Thus, despite difficulties such an approach might raise in term of subjects' motivation, it would be useful to test the performance at randomized, non-individualized difficulty levels. We are currently using such a protocol to further investigate the magnitude of age-related deterioration in PSI task performance, but the results are not available yet. Furthermore, as described above, we found the PSI task performance was correlated to the performance on a computer task of response inhibition only in young adults [30]. The lack of such correlation in older adults could be due to the variability in their performance on the PSI task. The large variability of older adults' performance

might stem from different executive function abilities, which we did not test in detail. We tested only the general cognitive state of our older adults using a MMSE questionnaire and, although none were cognitively impaired, detailed information on specific components of older adults' executive function might provide insight into potential causes of their variability in performing the PSI task. Namely, previous studies linking executive function to fall risk found that among older adults with relatively intact cognitive functions (i.e., high MMSE scores) differences in their executive function abilities occurred and these were predictive of future falls [47, 48]. Hence, additional investigation using more detailed information on the cognitive state of older adults, randomized difficulty levels of the PSI task, and, possibly, larger sample sizes is warranted.

Further insight into the precise role of response inhibition for obstacle avoidance could be obtained by synchronizing the congruent and incongruent Stroop task stimuli to obstacle presentation on the PSI task. Since only the incongruent stimuli require response inhibition, this would allow for an evaluation of its role during various stages of precision step inhibition. A similar approach was taken for avoidance of physical obstacles and largest differences in performance between congruent and incongruent stimuli were found during obstacle crossing [10]. If measures of muscle activity could be included in such a protocol, this might facilitate investigation of the underlying mechanisms, similar to the approach we took when investigating adjustments of tripping responses in Chapter 6.

One can avoid obstacles in several ways and it is not entirely clear what drives the underlying decision making. Our data indicate that the difference in ability to adjust leg movements in different directions might contribute to choosing a specific obstacle avoidance strategy. Further research should also look at whether it is possible to manipulate the success of leg movement adjustments in specific directions and, if these can be manipulated, would this impact strategy selection for obstacle avoidance.

A clinically relevant question would be whether a change in obstacle avoidance strategy selection would improve the success of obstacle avoidance and lead to reduced fall risk. For example, if step lengthening could be trained such that it is more successful than step shortening even under time pressure, would this result in step lengthening being used more for obstacle avoidance under time pressure? If so, would that make obstacle avoidance under time pressure more successful? Since obstacle avoidance is especially important for older adults, a large population at risk of falls [11], it is of interest to evaluate their ability to perform the dual-step paradigm presented in Chapter 4 and such research is currently being conducted by a colleague in our group (Mazaheri et al., in preparation). Additionally, potential differences between older and young adults might shed some light onto decision

making for obstacle avoidance, since older adults are known to prefer step lengthening more than young adults [9].

With respect to our experiment on tripping it would be of interest to use FZs of different characteristics to further explore the mechanisms driving leg movement adjustments in young adults. In the experiment presented here, we did not observe any step lengthening, which was probably due to the size of the FZ. Using a FZ of different size or cueing a specific direction of its avoidance by arrows might facilitate the use of different strategies. Smaller FZ might provide insights into decision making related to strategy choice, while cueing specific FZ avoidance directions might show if freely selected strategies correspond to those that are feasible for young adults. Finally, cueing a specific movement adjustment using a target landing zone instead of a FZ would help address the ability to execute specific leg movement adjustments during tripping.

So far we could only investigate the ability of older adults to adjust their unperturbed gait using the PSI task. Since tripping is one of the main causes of falls in this population [11, 149] future research should investigate whether older adults are still able to adjust their foot trajectories following tripping. If so, do they accomplish these adjustments using similar strategies and mechanisms as young adults? Furthermore, older adults often use recovery steps that are too short for successful balance recovery [82] and the question arises whether they can lengthen their trip recovery steps. As mentioned before, we observed no step lengthening in young adults, but the size of the FZ was a limiting factor. Therefore, cued FZ avoidance or the use of stepping targets instead of a FZ might be beneficial to answer this question. Finally, if older adults are able to adjust their steps, do they also demonstrate the learning effects observed in young adults? Such learning effects would enable teaching older adults to extend their trip recovery steps and might be promising for fall reduction [82]. The idea of utilizing learning for fall reduction is supported by recent research suggesting simple instructions can improve obstacle avoidance in older adults [183], behavior of older and young adults is modified following exposure or anticipation of upcoming trips or slips [82, 144, 158], as well as reports of reduced fall rates following perturbation training consisting of treadmill accelerations [145, 146]. Our findings of learning effects during leg movement adjustments on the PSI task and tripping, reported in Chapters 3, 5, and 6 also support such an idea.

Of course, older adults are not the only population at risk of falls and many patient populations are prone to falling [1–4, 70, 75]. Therefore, this approach could and should be extended to subjects suffering from various pathologies, such as stroke, Parkinson's disease, arthritis, cerebellar patients etc. Patients with neural damage that is well documented and localized might be of special interest, since combining neural imaging data with their performance could lead to localization of neural

structures related to leg movement adjustments. Namely, neural structures related to response inhibition and adjustments of arm movement have been widely investigated (see Appendix), mostly using functional magnetic resonance imaging (fMRI). For leg movements, this is however impossible to accomplish, given that it is not possible to walk in a MRI scanner. Hence, a promising, although technically challenging, approach to investigating neural mechanisms and structures underlying leg movement adjustments would be the use of electroencephalography in combination with the various tasks developed in this thesis.

Finally, aside from decision making for leg movement adjustments, another fundamental question exists. Is avoidance of obstacles fundamentally different from stepping to targets? This was reported for arm reaching, where fundamental differences were found between obstacle avoidance and hitting a target, although both situations required precisely the same movements [56]. This has not yet been studied in leg movements, but some discrepancies in the way step initiation to a target [50] and obstacle avoidance [58] are accomplished exist. Fast step initiation to a shifting target was suggested to rely on a direct visuomotor mapping in superior colliculi [50], which seems in contrast with equally fast movement adjustments reported for obstacle avoidance [58]. Tasks we developed in this thesis (and the approach of using visual context triggered by online data of subjects' behavior in general) might help address this issue if combined with detailed performance data, such as kinematics and electromyography. Contrasting behavior on the PSI task to leg movement adjustments following target shifts during precision stepping in the same subjects would provide insight into possible differences in the ways these adjustments are accomplished. Additionally, contrasting this performance to the ability to avoid the FZ or step into a target during trip recovery could help elucidate the underlying balance constraints.

Conclusions

This doctoral thesis addressed the ability to adjust leg movements during ongoing gait, both unperturbed and perturbed. Although previous research on the ability to adjust movements focused mostly on arm, eye, and simple leg movements (e.g., step initiation) our focus was on gait, because gait is one of the most common daily life circumstances requiring leg movement adjustments. Furthermore, gait is more complex than movements used previously and poses significant balance requirements, which could influence its adjustability. Such complexity makes this research especially challenging, but this thesis shows that it is possible to use well developed paradigms from the more advanced field of neural control of arm movements when investigating adjustments of ongoing gait. Two paradigms addressed in this thesis are the stop-signal paradigm, used to evaluate response inhibition, and double-step paradigm, used to evaluate online movement

corrections. While arm movement research typically focuses on one of these two paradigms, our work demonstrates both aspects (response inhibition and online corrections) are involved in adjustments of gait and should be taken into account.

In general, it is known that simple leg and arm movements can be adjusted extremely quickly. Our data complement this knowledge by showing that fast movement adjustments of ongoing gait, both unperturbed and perturbed, are also possible. Most of this thesis focused on the need to adjust landing position of an ongoing step in order to avoid obstacles. We complemented previous research by uncovering the role of response inhibition, which proved an important component of obstacle avoidance. Apparently, the ongoing step needs to be inhibited before a leg trajectory adjustment is made. In line with previous research, our findings confirm that response inhibition is global under time pressure and that obstacle avoidance interferes with cognitive tasks requiring inhibition of irrelevant information.

Step adjustments for obstacle avoidance proved possible even under extremely challenging circumstances, such as balance recovery following tripping. Balance recovery following tripping is a complex, whole body task and yet, subjects were able to initiate their movement adjustments with extremely short latencies, indicating subcortical origin of the initial response. While these adjustments were already possible in the first trial, indicating they can be executed as truly online corrections, in subsequent trials subjects relied on past experience and anticipation. Although this might make a focused investigation of online corrections difficult, it illustrates that neural control of movement is not made up of isolated mechanisms, but relies on their interaction. Perhaps even more importantly, the learning and anticipation effects observed in our studies of unperturbed and perturbed gait were beneficial for performance and show it is possible to improve leg movement adjustment abilities. Given the overall society aging this seems promising for fall prevention.

In conclusion, the work presented in this thesis adds to the knowledge on the ability of young and older adults to execute fast movement adjustments by showing these are also possible for ongoing gait, under time pressure, and in balance challenging conditions such as trip recovery. In our work we relied on the paradigms and knowledge from the more advanced field of arm movement motor control and believe these results illustrate the benefits and the importance of bridging the gap between leg and arm movement motor control research.

8 APPENDIX: NEURAL CONTROL OF MOVEMENT ADJUSTMENTS

Online corrections in the double step paradigm

Vision is a dominant source of information about the environment and often guides our movements. However, the way we perceive visual information differs from the way it guides our movements and each involves a distinct neural pathway for processing visual information [120, 160, 184, 185], as shown in Figure 8.1. Vision-for-perception relies on a 'slow' ventral visual stream consisting of projections that lead from the primary visual cortex (V1) to the inferior regions of the occipito-temporal cortex. On the other hand, action is controlled by a 'fast' dorsal visual stream projecting from V1 to superior regions of the occipito-parietal cortex and terminating at the posterior parietal cortex (PPC). Furthermore, there is evidence that visual information in the dorsal stream does not originate exclusively from V1. Other inputs to the dorsal stream probably depend on projections that bypass the geniculostriate pathway, such as those going from the eye to the superior colliculus, the interlaminar layers of the dorsal lateral geniculate nucleus or even directly to the pulvinar [184]. Although both streams interact in daily life, skilled action and its real-time 'bottom-up' adjustments in face of changing environment are controlled primarily by the dorsal stream [185].

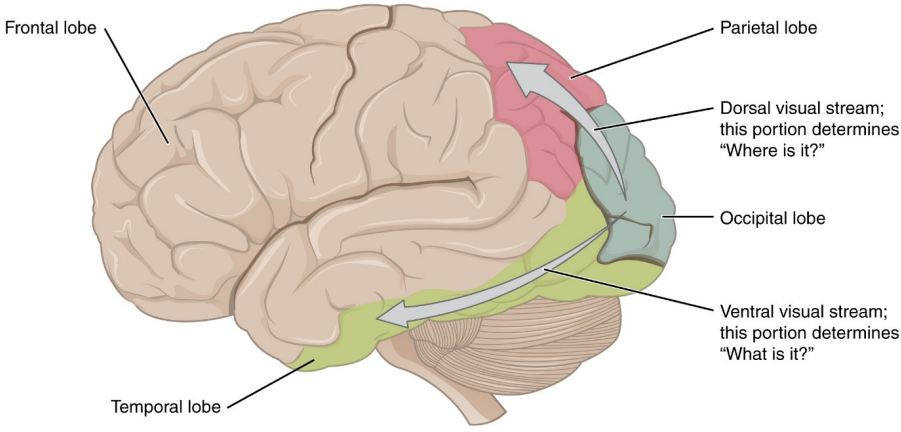

Figure 8.1. Two separate visual streams in the human brain. Fast dorsal visual stream guides action, while slower ventral visual streams guides perception. Image courtesy of Rice University under a Creative Commons Attribution License 4.0; downloaded from http://tinyurl.com/ng3u85y on March 30 2015.

Studies using double-step paradigm to investigate arm movements towards a target found that arm movement corrections can be executed without significantly prolonging movement duration. They even escape conscious control, as

demonstrated by the inability of subjects to reach in the opposite direction or to stop their movements in response to a target jump [122]. An explanation for such finding is that a typical double step paradigm involves a change in reaching target's position which occurs, for example, during the saccade to the target [139]. When a subject is asked to point to a peripheral target, the initial motor command is based on extra-foveal visual signal and eye and arm muscles are activated almost simultaneously [139]. Near the end of the saccade, the target location is recomputed using the (now available) more precise foveal visual information and compared to the arm location based on proprioception and the efferent copy of the motor command. The detected error is used to update the ongoing arm trajectory. Since this recalculation based on the visual information available at the end of the saccade occurs even if there was no target jump, a target jump during the saccade only adds to the initial movement planning error and a fast online correction does not result in prolonged movement times [139]. Temporal characteristics of such movement responses indicate that fast corrections of reaching are automatic, as if the hand is 'drawn' to the target irrespective of the subject's intention. However, movements that last longer seem to be under conscious control and they can be executed according to the task instructions [19, 122].

Key structure implicated in many studies on fast adjustments of arm movements is the posterior parietal cortex (PPC) [15, 122, 139, 186–188]. A study involving positron emission tomography (PET) imaging found significant activations of the PPC (specifically, intraparietal sulcus and the surrounding cortex), pontine nuclei, and the cerebellum during pointing movements in a double-step pointing paradigm performed without visual guidance (i.e., in the dark). Similarly, transcranial magnetic stimulation over the PPC disturbed the ability to correct contralateral arm movements when applied at movement onset [139] and a patient with bilateral PPC damage could only execute slow and intentional movement corrections [122], indicating a specific role for the PPC in fast automatic movement corrections.

The presumed role of the PPC is suggested to be related to error detection during ongoing movements [15, 186–188]. This error detection during pointing presumably relies on the representation of target and arm location through various afferent information (visual, proprioceptive, vestibular). The PPC transforms visual information on the target and arm locations into a common frame of reference using eye-centered coordinates [189, 190] and combines it with the forward model of the movement to calculate the error signal [186]. Support for such mechanism is found in the fact that the PPC activity is modulated as the arm approaches the target, i.e., as the reaching error changes [186]. Furthermore, PPC is connected to the main motor structures, which can act upon the error signal.

Once the error signal is calculated it is transformed into a motor command, presumably by the cerebellum [186], which receives input from the PPC via the

pontine nuclei. The cerebellum performs the inverse computations transforming the desired correction into a muscle command. Once such calculation is performed, the cerebellar signal influences the ongoing motor command by modulation of the neural signal issued by the primary motor cortex [186]. This is not the only reason cerebellum is important for movement corrections. Namely, the cerebellum is also responsible for forward modelling, i.e., estimation of the position and velocity of the arm based on the original motor command [188]. Deficits observed in cerebellar patients, who exhibit problems with online visuomotor movement control, illustrate its importance for movement correction [15, 188, 191, 192].

Additionally, alternative pathways might exist for fast movement corrections. The role of subcortical structures, possibly superior colliculi (SC), which receive direct retinal input (Figure 8.2) and are capable of a direct visuomotor mapping to upper limb movements, was indicated by a lack of additional interhemispheric transfer time in a split brain patient performing movement corrections in response to a target shift in the hemisphere contralateral to the pointing arm [193] and is supported by fMRI data confirming SC are activated during contralateral arm reaching [194, 195] and animal studies in cats and monkeys [15].

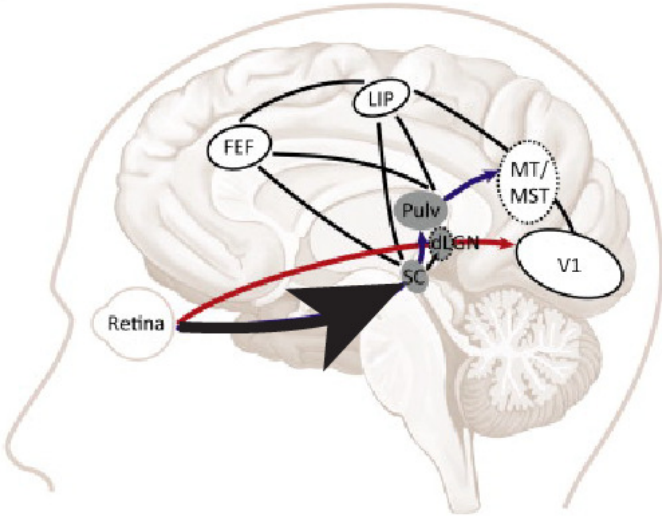

Figure 8.2. Direct visual pathway to superior colliculus (SC), denoted by the thick arrow. This retinocollicular pathway is a subcortical route that can bypass the dorsal lateral geniculate nucleus (dLGN) and V1 since it connects the retina to superior colliculus (SC) and pulvinar (Pulv) directly. From there visual information can be passed on to the middle- temporal area (MT) and medial-superior temporal area (MST), or to cortical areas involved in eye movement control (frontal eye field, FEF and lateral intraparietal sulcus, LIP). Adapted from [199], with permission.

While most research focused on fast, automatic movement corrections driven by visual information on target position, slower corrections are also possible and involve other pathways. For example, in an experiment which triggered a movement adjustment by a change in the color of the target, only slow, intentional corrections were made, and these could be performed by a patient with PPC lesions [122]. In line with that finding, another study found prolonged latencies of movement adjustments triggered by target color, form, and texture compared to luminance, orientation, and size [196]. Further illustrating that separate mechanisms drive fast automatic and slower intentional movement adjustments, no basal ganglia PET activity was found during fast movement corrections [186] and Parkinson's disease patients are able to adapt to double-step paradigm target jumps by generating smooth movements adjustments [197]. However, the same patients were unable to generate corrective submovements to large consciously detected target shifts [197], supporting the importance of basal ganglia for generation of corrective submovements. It was proposed that basal ganglia play a role in deciding if and when a corrective submovement is to be initiated [198].

Such findings indicate that the movement correction processes probably rely on a range of responses, from fast, automatic subcortical and/or visuomotor cortical responses involving the dorsal visual stream to slower, intentional responses probably involving the ventral visual stream [122]. These mechanisms might depend on the characteristics of the required correction and rely on different neural structures. If an appropriate correction can be achieved by a smooth modulation of the ongoing motor plan, it might utilize the fast subcortical and/or dorsal stream mechanisms, resulting in automatic corrections. On the other hand, if larger corrections, requiring perceptual processing of stimuli or generation of corrective submovements are needed they might rely on slower pathways and inhibition of the automatic correction response [197].

Response inhibition in the stop-signal paradigm

Various forms of inhibition exists and overlapping activity foci were often found for cognitive and motor inhibition [200]. However, response inhibition is usually tested using the stop-signal paradigm, in which responses are cancelled, or the go/no-go paradigm, in which responses are withheld. Both paradigms were found to involve some overlapping brain regions, but some differences in neural activation exist [200, 201]. Since movement cancelation is more relevant for this thesis, we focus on the neural structures involved in response inhibition in the stop-signal paradigm.

In general, response inhibition is driven by the activity of prefrontal cortex, which presumably generates the stopping command based on sensory information [200, 202]. Two regions especially highlighted are the right inferior frontal cortex (rIFC)

and some motor areas such as supplementary motor area (SMA), especially presupplementary motor area (preSMA) [200, 202–204]. They are believed to send a stop command via the basal ganglia to the primary motor cortex (M1) [27, 200, 202, 203, 205].

The functional role of the rIFC is not entirely clear, but it is suggested that its dorsal region, the right inferior frontal junction implements attentional detection, while its ventral sector, the posterior inferior frontal gyrus region (rIFG), implements inhibitory control via inputs to the basal ganglia. These two roles might be complementary, since the stop signal needs to be detected before it can trigger stopping. While numerous studies found rIFC to be important for response inhibition [200, 202–204, 206], some also report the bilateral activation of adjacent insula [200, 201, 204, 207]. For example, a meta-analysis of 21 studies using the stop-signal task did not find activity in the rIFG , but found activity of bilateral insulae instead [201]. The authors suggest that this discrepancy might be due to the fact that insula could be interpreted as rIFG in imaging studies [201]. The second important area involved in inhibition is the SMA and preSMA. The preSMA is connected with the rIFC, but also with the basal ganglia input nuclei – the striatum and subthalamic nucleus, making it a suitable candidate for a key role in response inhibition. Based on the role of preSMA in selecting sets of action-selection rules, motivation, conflict resolution, and modulating response thresholds, it was proposed that the SMA generates an inhibitory control signal to trigger the rIFG, which implements the inhibitory control via M1 [202]. Further support for the predominant role of the SMA came from the finding that rIFG seems to be critical for response inhibition only under conflicting circumstances, as demonstrated by a transcranial magnetic stimulation (TMS) study reporting impaired response inhibition following rIFG stimulation only when the stop-signal was combined with incongruent flankers [206]. In contrast, in a study using another version of the stop-signal task TMS stimulation of rIFC altered SMA activation, but not the other way around, indicating control is exerted in the opposite direction and rIFC is the dominant structure [208]. These discrepancies indicate that, while SMA is clearly important for stopping, the underlying mechanism and the relationship between rIFC and SMA requires further investigation and might depend heavily on the characteristics of the inhibitory task used.

Once the inhibitory signal is generated it probably travels to the subthalamic nucleus (STN), an input structure of the basal ganglia, which receives direct input from the preSMA and rIFC via a fast ‘hyperdirect pathway’ (enabling activation under less than 10 ms). STN broadly excites the globus pallidus pars interna, thus increasing the neural inhibition on thalamocortical output, which leads to general inhibition of the basal ganglia output and, hence, the motor system [110, 202]. Such widespread effects would be in line with global response inhibition effects found on the stop-signal task performed under time pressure [110, 203, 209]. However, an experiment

using a task lacking the element of choice on the 'go' trials found activity of an alternative, striatal pathway, indicating STN might not be the only pathway involved in global response inhibition [208].

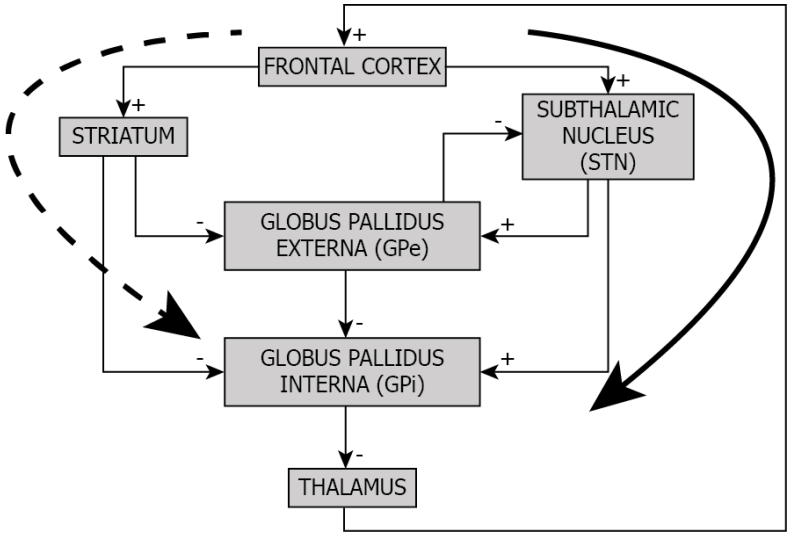

Figure 8.3. Response inhibition pathways, based on [203, 210]. Hyperdirect pathway is denoted by the thick solid arrow, direct striatal pathway is denoted by the thick dashed arrow. '+' denotes excitatory and '-' inhibitory connections.

Although it is more difficult, movements can be also be inhibited selectively. If subjects do not know in advance which movements might require inhibition, or do not prepare to stop, they most likely use global inhibitory mechanism to stop all movements and then selectively disinhibit movements to be continued [27, 28, 209]. On the other hand, if anticipation is involved (i.e., if the subjects use advance cues as to what movement might require inhibition), this is no longer the case [211][212]. In the latter case, proactive inhibition is coupled by activity in the SMA and striatum [202, 209, 211, 213] and it was proposed that the underlying mechanism involves adjusting the response threshold (i.e., threshold of M1) in anticipation of the stop-signal [202, 212]. Furthermore, when a stop signal was anticipated due to a cue preceding the 'go' signal, anticipatory inhibitory activity in the SMA and the striatum started immediately following the cue, indicating subjects started proactively inhibiting their responses because they expected a stop-signal. On the other hand, activity of the right inferior parietal cortex and rIFC was found only later, following the 'go' stimuli on trials in which no response inhibition was required. In these trials, as time from the 'go' stimuli passed, it became clear the subject's expectations were

violated since no stop-signal occurred [212]. Therefore, the authors suggest that rIFC might not be related to response inhibition per se, as many reported previously [200, 202–204, 206], but rather to a violation of expectations [212]. If this were the case, rIFC activity occurring on stop trials reported in previous studies on global inhibition [200, 202–204, 206] could also be explained as a violation of expectations: in those trial the stop-signal was not expected, but it occurred. This proposal [212] calls for future work, but illustrates the difficulties of disentangling the mechanisms driving response inhibition under various circumstances.

In conclusion, the precise response inhibition mechanisms and pathways are not entirely clear, but a general overview is given in Figure 8.3. Conflicting findings and many regions implicated in various inhibitory tasks indicate the importance of specific task demands [28, 200, 204, 207, 211, 212]. However, overlapping findings from stop-signal and go/no-go paradigm indicate key roles of SMA, pre-SMA, and rIFC (or insula) in canceling or withholding responses. Inhibition is most likely accomplished by rIFC and SMA changing the excitatory drive to the M1 via the basal ganglia, but when the STN or the striatum are used as pathways remains to be elucidated and probably depends on the task characteristics.

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APPOSITIONS

Human movement science and neuroscience benefit from participation of interdisciplinary experts, such as those with various engineering backgrounds.

Although seemingly an idealistic occupation, scientists are at a high risk of burnout, a psychological syndrome in response to chronic job related stressors. Therefore, resilience seems an essential skill for a successful scientist.

General public is not sufficiently aware that exercise, even when forced, promotes resilience, reduces anxiety, and protects against negative emotional consequences of stress by reducing its immediate effects and enhancing stress recovery.

CURRICULUM VITAE

Zrinka Potočanac was born on June 9 1984 in Ivanić Grad, Croatia. After finishing a mathematical gymnasium (MIOC) in Zagreb, she completed a Master's degree in Computer Science at University of Zagreb, Faculty of Electrical Engineering and Computing with a thesis focused on the analysis of electromyographical signals. Her career started at the Faculty of Electrical Engineering and Computing, where she worked as a research assistant, and continued in Information Technology and banking industries. Due to an interest in human movement science, she decided to pursue a career in science and was awarded a fellowship to join the first generation of MOVE-AGE, an Erasmus Mundus Joint Doctorate program. In September 2011 she moved to Belgium to commence her doctoral training in the Movement Control & Neuroplasticity Research Group of KU Leuven, under supervision of Jacques Duysens and Sabine Verschueren. Being a joint PhD project, her doctoral training also included a period of six months at the MOVE Research Institute, VU University in Amsterdam, where she worked in the Musculoskeletal Biomechanics Research group under supervision of Mirjam Pijnappels and Jaap van Dieën. The work performed within her joint doctoral degree project at KU Leuven and VU University Amsterdam is presented in this thesis. Starting from July 2015 she will work at the Department of Automation, Biocybernetics and Robotics of Jozef Stefan Institute, Slovenia.

LIST OF PUBLICATIONS

Publications in peer-reviewed journals

Potocanac Z., Pijnappels M., Verschueren S. M. P., van Dieën J., Duysens J. (2015). Two stage responses drive leg movement adjustments during trip recovery. *Journal of Neurophysiology, accepted pending revisions*

Mazaheri M., Hoogkamer W., **Potocanac Z.**, Verschueren S., Roerdink M., Beek P.J., Peper C.E. , Duysens J. (2015). Effects of ageing on the attentional demands of step adjustments to perturbations in visually cued walking. *The Journals of Gerontology: Medical Sciences, submitted*

Hoogkamer W., **Potocanac Z.**, Duysens J. (2015). Quick foot placement adjustments during gait: direction matters. *Experimental Brain Research, accepted pending revisions*

Hoogkamer W., Bruijn S., **Potocanac Z.**, Van Calenbergh F., Swinnen S., Duysens J. (2015) Split-belt walking in cerebellar lesion patients II: Role of somatosensory perception. *Journal of Neurophysiology, accepted pending revision*

Potocanac Z., Smulders E., Pijnappels M., Verschueren S. M. P., Duysens J. (2015). Response inhibition and avoidance of virtual obstacles during gait in healthy young and older adults. *Human Movement Science*, 39, 27-40.

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Potocanac, Z., Hoogkamer, W., Carpes, F. P., Pijnappels, M., Verschueren, S. M. P., Duysens, J. (2014). Response inhibition during avoidance of virtual obstacles while walking. *Gait & Posture*, 39(1), 641–4.

Duysens J., **Potocanac Z.**, Hegeman J., Verschueren S., McFadyen B.J. (2012) Split-second decisions on a split-belt; does limping affect obstacle avoidance? *Experimental Brain Research*, 223(1), 33-42.

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Abstracts of conference presentations

Hoogkamer W., **Potocanac Z.**, van Calenbergh F., Duysens J. "Online gait adjustments in cerebellar patients", Rocky Mountain Chapter of American Society of Biomechanics Conference, Estes Park, Colorado, USA, April 17 2015

Potocanac Z., van Dieen J., Verschueren S., Duysens J., Pijnappels M. "Very fast muscle activations during adjustment of tripping responses", 4th World Congress of International Society for Posture and Gait Research, Seville, Spain, June 28-July 2 2015, accepted

Mazaheri M., Hoogkamer W., **Potocanac Z.**, Verschueren S., Roerdink M., Beek PJ., Peper CL., Duysens J. "Ageing effects on attentional demands of stepping adjustment in response to visual target shifts" 4th World Congress of International Society for Posture and Gait Research, Seville, Spain, June 28-July 2 2015, accepted

Potocanac Z., Pijnappels M, Verschueren S., van Dieën J., Duysens J. "Timing of fast online corrections to tripping perturbations", Neuroscience 2014, Washington DC, USA, November 15-19 2014

Potocanac Z., Smulders E., Pijnappels M., Verschueren S. M. P., Duysens J. "Response inhibition measured using a walking task is correlated to a computer inhibition test in young adults", Society for Neural Control of Movement 24th annual meeting, Amstedam, the Netherlands, April 22-25 2014

Potocanac Z., van Dieën J., Verschueren S., Duysens J., Pijnappels M. "Online step adjustments during unexpected tripping", 7th International scientific conference on Kinesiology 2014, Opatija, Croatia, May 22-25 2014

Potocanac Z., van Dieën J., Verschueren S., Duysens J., Pijnappels M. "Can young adults adjust their recovery step during unexpected tripping?", 3rd World Congress of International Society for Posture and Gait Research, Vancouver, Canada, June 29-July 3 2014

Mohammadi F., **Potocanac Z.**, Bruijn S.M., Verschueren S., Nieuwboer A. "The effect of concurrent cognitive loading and asymmetric walking in patients with Parkinson`s disease with and without freezing of gait", 3rd World Congress of International Society for Posture and Gait Research, Vancouver, Canada, June 29-July 3 2014

Potocanac Z., Smulders E., Hoogkamer W., Pijnappels M., Verschueren S. M. P., Duysens J. "Response inhibition during avoidance of virtual obstacles", Belgian society for Kinesiology (Vereniging voor Kinesiologie) 18th annual conference, Leuven, Belgium, December 13th 2013

Hoogkamer W., **Potocanac Z.**, Uniszkiewicz D., Dierckxsens S., Swinnen S.P., Duysens J. "Functional split-belt test: relation between perception and adaptation", Belgian society for Kinesiology (Vereniging voor Kinesiologie) 18th annual conference, Leuven, Belgium, December 13th 2013

Potocanac Z., Smulders E., Hoogkamer W., Pijnappels M., Verschueren S. M. P., Duysens J. "Is response inhibition during obstacle avoidance while walking the same as response inhibition measured manually or with a dual task?", 11th Motor Control and Human Skill Conference, Melbourne, Australia, November 27-29 2013

Potocanac Z., Smulders E., Carpes F., Hoogkamer W., Pijnappels M., Verschueren S, Duysens J. “Avoiding virtual obstacles during walking: testing response inhibition”, XXIV International Society of Biomechanics Congress, Natal, Brazil, August 4-9 2013

Potocanac Z., Smulders E., Pijnappels M., Verschueren S., Duysens J. “Older adults perform worse than young in a dual task when response inhibition is required”, 2nd Joint World Congress of International Society for Posture and Gait Research and Gait & Mental Function, Akita, Japan, June 22-26 2013

Hoogkamer W., **Potocanac Z.**, Uniszkiewicz D., Dierckxsens S., Swinnen S.P., Duysens J. “Early rate of split-belt adaptation is related to somatosensory perception”, 2nd Joint World Congress of International Society for Posture and Gait Research and Gait & Mental Function, Akita, Japan, June 22-26 2013

Potocanac Z., Nienhuis B., Leunissen I., Coxon J., Swinnen S., Duysens J. "Response inhibition during a walking task compared to upper limb computer inhibition tests.", 2013 Annual meeting of the Society for cognitive neuroscience, San Francisco, CA, April 13-16 2013

Biljan B., **Potocanac Z.,** Cifrek M. (2011) Comparison of Two Muscle Activity Detection Techniques from Surface EMG Signals Applied to Countermovement Jump. 5th European Conference of the International Federation for Medical and Biological Engineering. Budapest, Hungary, September 14-18 2011

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'The world is busting at its seams
and you're just a prisoner of your dreams'[1]

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[1] Springsteen B. Night. Born to Run, track #1, 1975.